# FY 2013

## *PERFORMANCE REPORT TO THE PRESIDENT AND CONGRESS*

*for the*

# *Prescription Drug User Fee Act*

**Food and Drug Administration**
**Department of Health and Human Services**

# *Commissioner's Report*

I am pleased to present to the President and Congress the Food and Drug Administration's (FDA) fiscal year (FY) 2013 Prescription Drug User Fee Act (PDUFA) Performance Report. This report marks the 21st year of PDUFA and the first year of PDUFA V (FY 2013 through FY 2017).

This report details FDA's final performance for the fifth and final year of PDUFA IV (FY 2012) and preliminary performance for the first year of PDUFA V (FY 2013). FDA met or exceeded 11 of 12 performance goals in FY 2012. Similarly, preliminary results of reviews completed in FY 2013 indicate that FDA has the potential to meet or exceed almost all (11 of 12) review performance goals again for FY 2013.

In addition to meeting performance goals, FDA's estimated median approval times for priority and standard new drug applications (NDAs) and biologics license applications (BLAs) continued to improve, with median priority application review times at or less than 6 months for both FY 2011 and FY 2012. The percentage of standard applications approved during the first review cycle also increased to the highest levels ever recorded in FY 2012.

We are committed to meeting all PDUFA performance goals related to human drug review. Although FDA realized higher performance levels and met more procedural goals than ever before in FY 2012, FDA continues to strengthen efforts to improve performance in these areas while maintaining a focus on ensuring that safe, effective, and high-quality new drugs and biologics are reviewed in an efficient and predictable time frame.

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs

# *Acronyms*

**BLA** – Biologics License Application

**CBER** – Center for Biologics Evaluation and Research

**CDER** – Center for Drug Evaluation and Research

**FAERS** – FDA Adverse Event Reporting System

**FBIS** – FAERS Business Intelligence Solution

**FDA** – Food and Drug Administration

**FDASIA** – Food and Drug Administration Safety and Innovation Act

**FY** – Fiscal Year (October 1 to September 30)

**ICH** – International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use

**IND** – Investigational New Drug

**MedDRA** – Medical Dictionary for Regulatory Activities

**NDA** – New Drug Application

**NME** – New Molecular Entity

**PDUFA –** Prescription Drug User Fee Act

**PEPFAR** – President's Emergency Plan for AIDS Relief

**PFDD** – Patient-Focused Drug Development

**PMC** – Postmarketing Commitment

**PMR** – Postmarketing Requirement

**REMS** – Risk Evaluation and Mitigation Strategy

# *Executive Summary*

PDUFA was enacted in 1992 and authorized FDA to collect user fees from pharmaceutical and biotechnology companies for the review of certain human drug and biological products. In return, FDA commits to certain review performance goals and procedural and processing goals and commitments, agreed to with industry.

PDUFA must be reauthorized by Congress every 5 years, or the program will expire. The fifth and most recent authorization (known as PDUFA V) occurred on July 9, 2012, when the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA). As directed by Congress in the FDA Amendments Act of 2007, FDA developed proposed enhancements for PDUFA V in consultation with drug industry representatives, patient and consumer advocates, health care professionals, and other public stakeholders. These discussions led to the current set of performance goals for the FY 2013-2017 period, detailed in a document commonly known as the PDUFA Commitment Letter.[1]

This report summarizes FDA's performance in meeting PDUFA goals and commitments for FY 2012, the final year of PDUFA IV, and FY 2013, the first year under PDUFA V. Specifically, it updates and finalizes performance data for submissions received in FY 2012 and initially reported in the FY 2012 PDUFA Performance Report and presents preliminary data on FDA's progress in meeting FY 2013 goals. Updates on FDA accomplishments related to additional PDUFA V commitments for FY 2013 are also included. Details of FY 2012 and FY 2013 performance, review cycle data on all original NDAs and BLAs approved during FY 2013, the number of applications filed by review division, historical review trend data, and definitions of key terms used in this report are presented in the appendices. Descriptions of the various application types are included on page 4.

## Achievements in FY 2013

Among the changes made under PDUFA V, FDA has established a new review program (the Program) for new molecular entity (NME) NDAs and original BLAs received from October 1, 2012, through September 30, 2017. The goals of the Program are to increase the efficiency and effectiveness of the first review cycle and decrease the number of review cycles necessary for approval by providing (1) new opportunities for communication between applicants and the FDA review team during FDA's review of the application and (2) additional review time for FDA and applicants to address review activities that occur late in the review cycle for these highly complex applications. During FY 2013, 54 applications were received and will be reviewed under the Program. As of September 30, 2013, six of these applications had been reviewed and acted on, and all of these reviews were completed on time.

[1] www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf

FDA's estimated median approval times for priority and standard NDAs and BLAs continued to improve, with median priority application review times less than or equal to 6 months for both the FY 2011 and FY 2012 cohorts. (It is too soon to assess approval times for the FY 2013 cohort.) The percentage of standard applications filed in FY 2012 and approved during the first review cycle also increased to the highest levels ever recorded.

## Review Performance

The FY 2012 cohort had a workload of 2,780 review actions. FDA exceeded the 90 percent performance level for 11 of 12 of the review performance goals.

For FY 2013, FDA is currently meeting or exceeding 10 of 12 review performance goals. With 1,166 submissions currently under review and within the PDUFA goal date (on time), FDA has the potential to meet or exceed 11 of 12 review performance goals for FY 2013.

## Procedural and Processing Performance

FDA's workload for actions related to procedural and processing goals and commitments (i.e., meeting management, procedural responses, and procedural notifications) for the FY 2012 cohort was 7,352. FDA exceeded the 90 percent performance level for 13 of 18 of the procedural and processing goals.

FDA is currently meeting or exceeding 9 of 18 procedural and processing goals for the FY 2013 cohort. With 897 submissions currently under review and within the PDUFA goal date (on time), FDA has the potential to meet or exceed 12 of 18 procedural and processing goals for FY 2013.

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# *Introduction*

On July 9, 2012, the President signed FDASIA into law, which included the reauthorization of PDUFA for FY 2013 through FY 2017, known as PDUFA V. PDUFA V continues to provide FDA with a consistent source of funding to help maintain a predictable and efficient review process for human drugs and biologics. In return for additional resources, FDA agreed to certain review performance goals, such as completing reviews of NDAs and BLAs and taking regulatory actions on them within predictable timeframes.

Since the implementation of PDUFA I in 1992, FDA has used PDUFA resources to significantly reduce the time it takes to evaluate new drugs without compromising its rigorous standards for demonstration of safety, efficacy, and quality of new drugs and biologics before approval. The efficiency gains under PDUFA have revolutionized the drug review process in the United States and have enabled FDA to ensure more timely access to innovative and important new therapies for patients.

More information on the history of PDUFA is available on the FDA website.[2]

## Information Presented in This Report

This report presents PDUFA workload and performance information for two different types of goals: (1) review of applications and submissions as well as preparation of documents and action letters related to FDA decisions and (2) meeting management and review goals related to procedural responses and notifications. PDUFA workload information for these goals is included in the tables that follow on pages 5 and 8. Significant additional components of PDUFA workload that are not captured by PDUFA goals and not presented in this report include review of investigational new drug (IND) applications, labeling supplements, annual reports, and the ongoing monitoring of drug safety in the postmarket setting.

PDUFA performance information related to achieving the two types of goals includes reviews of submissions pending from previous fiscal years as well as reviews of submissions received during the current fiscal year. This report presents final performance for FY 2012 cohort submissions based on actions completed in FY 2012 and FY 2013. In addition, it includes preliminary performance for FY 2013 cohort submissions that had actions completed or due for completion in FY 2013. Final performance for FY 2013 cohort submissions will be presented in the FY 2014 PDUFA Performance Report and will include actions for submissions still pending within the PDUFA goal date as of September 30, 2013.

Among other changes made under PDUFA V, FDA established a new review program (the

[2] www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/default.htm

Program) for NME NDAs and original BLAs received from October 1, 2012, through September 30, 2017. The goals of the Program are to increase the efficiency and effectiveness of the first review cycle and decrease the number of review cycles necessary for approval by providing (1) new opportunities for communication between applicants and the FDA review team during FDA's review of the application and (2) additional review time for FDA and applicants to address review activities that occur late in the review cycle for these highly complex applications. More information on FDA's achievements related to other PDUFA V commitments can be found on pages 13 through 17 of this report.

The following information refers to FDA performance presented in this report.

- The following terminology is used throughout this document:
  - *Application* means a new, original application
  - *Supplement* means a supplement to an approved application
  - *Resubmission* means a resubmitted application or supplement in response to a complete response, approvable, not approvable, or tentative approval letter
  - *NME* refers only to NMEs that are NDAs (not BLAs)
  - *Submission* applies to all of the above

- Under PDUFA V, the preliminary counts of NMEs in workload tables for the current FY may not be discrete filed NMEs. FDA often receives multiple submissions for the same NME (e.g., different dosage forms). All are initially designated as NMEs, and once FDA approves the first of the multiple submissions, the others will be designated as non-NMEs and workload numbers will be appropriately updated in later years.

- The IND data presented in this report do not include biosimilar INDs.

- FDA only files applications that are sufficiently complete to permit a substantive review. FDA makes a filing decision within 60 days of an original application's receipt. FDA's review of an application begins once the application is received. For NME NDAs and original BLAs reviewed under the PDUFA V NME Review Program (see the PDUFA V Commitment Letter[3] for more information), the PDUFA clock begins after the conclusion of the 60-day filing period. For all other submissions, the PDUFA clock begins upon FDA's receipt of the application.

- FDA reports PDUFA performance data annually for each fiscal year receipt cohort (defined as submissions filed from October 1 to September 30 of the following year). In each fiscal year, FDA receives submissions that will have associated goals due in the following fiscal year. In these cases, FDA's performance will be reported in subsequent fiscal years, either after FDA takes an action or when the goal becomes overdue, whichever comes first.

[3] www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf

- Submission types (e.g., responses to clinical holds) with shorter (e.g., 30 day) review-time goals tend to have a larger percentage of reviews completed by the end of the fiscal year, and their preliminary performance is a more reliable indicator of their final performance. However, submission types (e.g., standard efficacy supplement submissions) with longer (e.g., 10 month) review-time goals tend to have a smaller percentage of reviews completed, and their preliminary performance is a less reliable indicator of their final performance.

- Final performance for FY 2012 submissions is shown as the percentage of submissions that were reviewed within the specified goal timeline. Submission types with 90 percent or more submissions reviewed by the goal date are shown as having met the goal.

- Preliminary performance for FY 2013 submissions is shown as the percentage of submissions reviewed on time as of September 30, 2013, excluding actions pending within the PDUFA goal date. Submission types with 90 percent or more submissions reviewed by the goal date are shown as currently meeting the goal. The highest possible percent of reviews that may be completed on time (highest possible final performance) if all non-overdue pending reviews are completed within goal is also shown.

- FY 2013 workload and performance figures include applications that are identified as *undesignated*, which means they are still within the 60-day filing date and have not yet had a review priority designation made.

- For resubmitted applications, the applicable performance goal is determined by the year in which the resubmission is received, rather than the year in which the original application was submitted.

- Unless otherwise noted, all performance data are as of September 30, 2013.

- Definitions of key terms used throughout this report can be found in Appendix F.

## Submission Types Included in This Report

- **NDA –** When the sponsor of a new drug believes that enough evidence on the drug's safety and effectiveness has been obtained to meet FDA's requirements for marketing approval, the sponsor submits to FDA a new drug application (NDA). The application must contain data from specific technical viewpoints for review, including chemistry, pharmacology, medical, biopharmaceutics, and statistics. If the NDA is approved, the product may be marketed in the United States.
- **NME –** A new molecular entity (NME) is a drug for which the active ingredient has never before been approved or marketed in the United States in any form.
- **BLA –** A biologics license application (BLA) is a submission that contains specific information on the manufacturing processes, chemistry, pharmacology, clinical pharmacology, and the clinical effects of a biologic product. If the information provided meets FDA requirements, the application is approved and a license is issued allowing the firm to market the product.
- **Resubmission –** A resubmitted original application or supplement is a complete response to an FDA action letter that addresses all identified deficiencies.
- **Supplement –** A supplement is an application to allow a company to make changes in a product that already has an approved NDA or to seek FDA approval for new uses of an approved drug. CDER must approve all major NDA changes (in packaging or ingredients, for instance) to ensure the conditions originally set for the product are still met.

**Source:** www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm

# *PDUFA Review Goals*

## Review Workload: FY 2008 to FY 2013

In the table below, preliminary review workload numbers from FY 2013 are compared to the previous 5-year averages for original NDAs and BLAs, resubmissions, and supplements. Workload was lower than or equal to 5-year averages for all submission types except priority and standard NMEs and BLAs. Workload for original applications (priority and standard) will appear different from workload reported in previous years due to different reporting requirements under PDUFA V.

**Review Workload for Applications and Submissions**

| Submission Type | FY 08 | FY 09 | FY 10 | FY 11 | FY 12* | FY 13 | FY 08 to FY 12 5-Year Average | FY 13 Compared to 5-Year Average |
|---|---|---|---|---|---|---|---|---|
| Original Priority NMEs and BLAs | 17 | 17 | 11 | 14 | 18 | 19 | 15 | ↑27% |
| Original Standard NMEs and BLAs | 30 | 33 | 18 | 23 | 32 | 36 | 27 | ↑33% |
| Original Priority non-NME NDAs | 17 | 8 | 8 | 8 | 8 | 9 | 10 | ↓10% |
| Original Standard non-NME NDAs | 76 | 88 | 66 | 56 | 72 | 72 | 72 | ↔ |
| Class 1 Resubmitted NDAs and BLAs | 19 | 16 | 12 | 9 | 6 | 11 | 12 | ↓8% |
| Class 2 Resubmitted NDAs and BLAs | 38 | 54 | 41 | 53 | 36 | 40 | 44 | ↓9% |
| Priority NDA and BLA Efficacy Supplements | 39 | 42 | 19 | 23 | 39 | 30[†] | 32 | ↓6% |
| Standard NDA and BLA Efficacy Supplements | 112 | 117 | 125 | 118 | 108 | 112 | 116 | ↓3% |
| Class 1 Resubmitted NDA and BLA Efficacy Supplements | 12 | 8 | 17 | 13 | 4 | 2 | 11 | ↓82% |
| Class 2 Resubmitted NDA and BLA Efficacy Supplements | 32 | 27 | 17 | 24 | 19 | 9 | 24 | ↓63% |
| NDA and BLA Manufacturing Supplements requiring prior approval | 910 | 971 | 967 | 809 | 872 | 867[‡] | 906 | ↓4% |
| NDA and BLA Manufacturing Supplements not requiring prior approval | 1,638 | 1,605 | 1,524 | 1,771 | 1,566 | 1,521 | 1,621 | ↓6% |

* FY 2012 numbers were changed to reflect updates to data presented in the FY 2012 PDUFA Performance Report.

[†] FY 2013 numbers are preliminary. Three efficacy supplements included in the 'priority' row above have an undesignated review priority as of September 30, 2013, and will be updated in the FY 2014 PDUFA Performance Report.

[‡] FY 2013 numbers are preliminary. Two manufacturing supplements included in the 'requiring prior approval' row above have an undesignated review priority as of September 30, 2013, and will be updated in the FY 2014 PDUFA Performance Report.

## Final FY 2012 Review Performance

Final FY 2012 review goal performance is presented in the table below. Final performance for submission types that met the goal (with 90 percent or more reviews completed by the goal date) is shown in bold text. FDA exceeded the 90 percent performance level for 11 of 12 of the review performance goals in FY 2012. More detailed information on performance is available in Appendix A.

| Submission Type | Goal: Review 90 percent within | FY 2012 Performance |
|---|---|---|
| Original Priority NMEs and BLAs | 6 months | **94%** |
| Original Standard NMEs and BLAs | 10 months | **100%** |
| Original Priority NDAs and BLAs | 6 months | **96%** |
| Original Standard NDAs and BLAs | 10 months | **97%** |
| Class 1 Resubmitted NDAs and BLAs | 2 months | **100%** |
| Class 2 Resubmitted NDAs and BLAs | 6 months | **100%** |
| Priority NDA and BLA Efficacy Supplements | 6 months | **100%** |
| Standard NDA and BLA Efficacy Supplements | 10 months | **97%** |
| Class 1 Resubmitted NDA and BLA Efficacy Supplements | 2 months | **100%** |
| Class 2 Resubmitted NDA and BLA Efficacy Supplements | 6 months | 84% |
| NDA and BLA Manufacturing Supplements requiring prior approval | 4 months | **93%** |
| NDA and BLA Manufacturing Supplements not requiring prior approval | 6 months | **94%** |

## Preliminary FY 2013 Review Performance

Preliminary FY 2013 review goal performance is presented in the table below.

- The review progress (the number of reviews completed or pending overdue) and the total number of submissions received for each submission type are shown in the second column. Current performance for submission types with a greater proportion of reviews completed will be more representative of final performance. Appendix B contains additional information on the completed reviews.
- Applications reviewed under the Program have review goals starting from the 60-day filing date, while other submissions have goals starting from the submission receipt date.
- Current performance for submission types that are meeting the performance goal (90 percent or more reviews completed by the goal date) as of September 30, 2013, is shown in bold text. FDA is meeting or exceeding the 90 percent performance level for 10 of 12 of the review performance goals.
- If all non-overdue pending submissions are reviewed on time, FDA will achieve the performance presented in the Highest Possible Final Performance column. FDA has the potential to meet or exceed the 90 percent performance level for 11 of 12 review performance goals.

| Submission Type | Review Progress | Goal: Review 90 percent within | FY 2013 Current Performance | Highest Possible Final Performance |
|---|---|---|---|---|
| Original Priority NMEs and BLAs | 3 of 19 complete | 6 months from filing date | **100%** | 100% |
| Original Standard NMEs and BLAs | 3 of 36 complete | 10 months from filing date | **100%** | 100% |
| Original Priority non-NME NDAs* | 1 of 9 complete | 6 months | **100%** | 100% |
| Original Standard non-NME NDAs* | 7 of 72 complete | 10 months | **100%** | 100% |
| Class 1 Resubmitted NDAs and BLAs | 11 of 11 complete | 2 months | **100%** | 100% |
| Class 2 Resubmitted NDAs and BLAs | 20 of 40 complete | 6 months | **100%** | 100% |
| Priority NDA and BLA Efficacy Supplements | 12 of 27 complete | 6 months | **100%** | 100% |
| Standard NDA and BLA Efficacy Supplements | 25 of 112 complete | 10 months | 88% | 97% |
| Class 1 Resubmitted NDA and BLA Efficacy Supplements | 2 of 2 complete | 2 months | **100%** | 100% |
| Class 2 Resubmitted NDA and BLA Efficacy Supplements | 6 of 9 complete | 6 months | 83% | 89% |
| NDA and BLA Manufacturing Supplements requiring prior approval | 600 of 865 complete | 4 months | **92%** | 95% |
| NDA and BLA Manufacturing Supplements not requiring prior approval | 872 of 1,521 complete | 6 months | **96%** | 98% |

* Starting in FY 2013, under PDUFA V, FDA is required to report non-NME NDAs separately (instead of all NDAs and BLAs as reported in previous years).

# *PDUFA Procedural and Processing Goals and Commitments*

## Procedural and Processing Workload: FY 2008 to FY 2013

FY 2013 procedural and processing workload, which includes actions related to meeting management, procedural responses, and procedural notifications, is compared to the previous 5-year averages in the table below. FY 2013 workload varied greatly from past 5-year averages, with the largest difference seen in major dispute resolutions.

**Meeting Management, Procedural Responses, and Procedural Notifications Workload**

| Submission/Request Type | FY 08 | FY 09 | FY 10 | FY 11 | FY 12* | FY 13 | FY 08 to FY 12 5-Year Average | FY 13 Compared to 5-Year Average |
|---|---|---|---|---|---|---|---|---|
| Type A Meeting Requests | 362 | 222 | 234 | 204 | 184 | 188[†] | 241 | ↓22% |
| Type B Meeting Requests | 1,330 | 1,297 | 1,305 | 1,331 | 1,322 | 1,370 | 1,317 | ↑4% |
| Type C Meeting Requests | 652 | 673 | 718 | 715 | 785 | 888 | 709 | ↑25% |
| Type A Meetings Scheduled | 260 | 201 | 216 | 184 | 168 | 170[†] | 206 | ↓17% |
| Type B Meetings Scheduled | 1,157 | 1,148 | 1,199 | 1,263 | 1,261 | 1,176 | 1,206 | ↓2% |
| Type C Meetings Scheduled | 486 | 532 | 613 | 646 | 725 | 593 | 600 | ↓1% |
| Type B Written Response | -- | -- | -- | -- | -- | 148 | --[‡] | --[‡] |
| Type C Written Response | -- | -- | -- | -- | -- | 251 | --[‡] | --[‡] |
| Meeting Minutes | 1,515 | 1,518 | 1,580 | 1,526 | 1,585 | 1,418 | 1,545 | ↓8% |
| Responses To Clinical Holds | 213 | 221 | 204 | 176 | 178 | 162 | 198 | ↓18% |
| Major Dispute Resolutions | 14 | 15 | 7 | 18 | 32 | 29 | 17 | ↑71% |
| Special Protocol Assessments | 354 | 336 | 309 | 313 | 288 | 220 | 320 | ↓31% |
| Review of Proprietary Names Submitted During IND Phase | -- | 63 | 102 | 128 | 164 | 157 | 114[§] | ↑38% |
| Review of Proprietary Names Submitted with NDA/BLA | -- | 185 | 207 | 186 | 216 | 235 | 199[§] | ↑18% |
| First-Cycle Filing Review Notifications – NDAs and BLAs | 137 | 145 | 105 | 101 | 126 | 136 | 123 | ↑11% |
| First-Cycle Filing Review Notifications – Efficacy Supplements | 122 | 116 | 112 | 95 | 96 | 93 | 108 | ↓14% |
| Notification of Planned Review Timelines – NDAs and BLAs | -- | -- | -- | 101 | 126 | 136 | --[‡] | --[‡] |
| Notification of Planned Review Timelines – Efficacy Supplements | -- | -- | -- | -- | 96 | 93 | --[‡] | --[‡] |

* FY 2012 numbers were changed to reflect updates to data presented in the FY 2012 PDUFA Performance Report.
[†] Includes meetings denoted as undesignated in the database.
[‡] Due to changing reporting requirements, no past year average is presented for this area.
[§] This information was not tracked prior to FY 2009, so in place of a 5-year average, a 4-year average is presented.

## Final FY 2012 Procedural and Processing Performance

The table below presents final performance for FY 2012 submissions in meeting goals related to meeting management, procedural responses, and procedural notifications as outlined under PDUFA IV. Final performance for submission types that met the goal (90 percent or more reviews completed by the goal date) is shown in bold text. FDA exceeded the 90 percent performance level for 13 of 18 of the procedural and processing goals in FY 2012. More detailed information on performance is available in Appendix A.

| Submission/Request Type | Goal: Review 90 percent within | FY 2012 Performance |
|---|---|---|
| Type A Meeting Requests | 14 days | 85% |
| Type B Meeting Requests | 21 days | 85% |
| Type C Meeting Requests | 21 days | 87% |
| Type A Meetings Scheduled | 30 days | **94%** |
| Type B Meetings Scheduled | 60 days | **93%** |
| Type C Meetings Scheduled | 75 days | **91%** |
| Meeting Minutes | 30 days | 85% |
| Responses to Clinical Holds | 30 days | 88% |
| Major Dispute Resolutions | 30 days | **97%** |
| Special Protocol Assessments | 45 days | **90%** |
| Review of Proprietary Names Submitted During IND Phase | 180 days | **99%** |
| Review of Proprietary Names Submitted with NDA/BLA | 90 days | **99%** |
| First-Cycle Filing Review Notifications: Original NDAs and BLAs | 74 days | **97%** |
| First-Cycle Filing Review Notifications: Efficacy Supplements | 74 days | **94%** |
| Notification of Planned Review Timelines: Original NMEs and BLAs | 74 days | **96%** |
| Notification of Planned Review Timelines: All Original NDAs and BLAs | 74 days | **98%** |
| Notification of Planned Review Timelines: Efficacy Supplements for New/Expanded Indications | 74 days | **93%** |
| Notification of Planned Review Timelines: All Efficacy Supplements | 74 days | **95%** |

## Preliminary FY 2013 Procedural and Processing Performance

The table below presents preliminary performance for FY 2013 submissions in meeting goals related to meeting management, procedural responses, and procedural notifications as outlined under PDUFA V.

- The review progress (the number of reviews completed or pending overdue) and the total number of submissions received for each submission type are shown in the second column. Current performance for submission types with a greater proportion of reviews completed will be more representative of final performance. More detailed information on the completed reviews is available in Appendix B.
- Current performance for submission types that are meeting the goal (with 90 percent or more reviews completed by the goal date) as of September 30, 2013, is shown in bold text. FDA is currently meeting or exceeding 9 of 18 procedural and processing goals.
- If all pending submissions are reviewed on time, FDA has the potential to meet 12 of 18 goals, as seen in the Highest Possible Final Performance column.

| Submission/Request Type | Review Progress | Goal: Review 90 percent within | FY 2013 Current Performance | Highest Possible Final Performance |
|---|---|---|---|---|
| Type A Meeting Requests | 146 of 188 complete | 14 days | 84% | 88% |
| Type B Meeting Requests | 1,347 of 1,370 complete | 21 days | 89% | 89% |
| Type C Meeting Requests | 870 of 888 complete | 21 days | 87% | 87% |
| Type A Meetings Scheduled | 121 of 170 complete | 30 days | 88% | 91% |
| Type B Meetings Scheduled | 1,116 of 1,176 complete | 60 days | **92%** | 92% |
| Type C Meetings Scheduled | 545 of 593 complete | 75 days | **92%** | 93% |
| Type B Written Response | 124 of 148 complete | 60 days | 69% | 74% |
| Type C Written Response | 195 of 251 complete | 75 days | 78% | 83% |
| Meeting Minutes | 1,067 of 1,418 complete | 30 days | 88% | 91% |
| Responses to Clinical Holds | 154 of 162 complete | 30 days | 88% | 89% |
| Major Dispute Resolutions | 21 of 29 complete | 30 days | **100%** | 100% |
| Special Protocol Assessments | 198 of 220 complete | 45 days | **93%** | 94% |
| Review of Proprietary Names Submitted During IND Phase | 99 of 157 complete | 180 days | **96%** | 97% |
| Review of Proprietary Names Submitted with NDA/BLA | 206 of 235 complete | 90 days | **98%** | 98% |
| First-Cycle Filing Review Notifications: Original NDAs and BLAs | 102 of 136 complete | 74 days | **98%** | 99% |
| First-Cycle Filing Review Notifications: Efficacy Supplements | 74 of 93 complete | 74 days | 89% | 91% |
| Notification of Planned Review Timelines: Original NDAs and BLAs | 110 of 136 complete | 74 days | **100%** | 100% |
| Notification of Planned Review Timelines: Efficacy Supplements | 71 of 93 complete | 74 days | **94%** | 96% |

## Meeting Planned Review Timeline Target Dates

FDA has committed to inform applicants of the planned timeline for feedback related to labeling as well as postmarketing requirements (PMRs) and postmarketing commitments (PMCs). This timeline must be included in a letter sent within 14 days following the 60-day filing date (known as a 74-day letter). FDA committed to report its performance in meeting the planned review timelines for communication of labeling comments and PMR/PMC requirements/requests, though there is no PDUFA-related goal. This commitment includes reporting on the number and percentage of applications for which the planned target dates for communication of labeling comments and PMRs/PMCs were met. If FDA receives a major amendment after issuing the 74-day letter, the timeline included is no longer applicable.

### *Final FY 2012 Cohort Performance*

| Application Type | Number of 74-Day Letters With Timelines | Target Date Inapplicable | Target Date Met | Target Date Not Met | Withdrawn | Percent of Applications Target Date Met* |
|---|---|---|---|---|---|---|
| NMEs and BLAs | 46 | 1 | 33 | 11 | 1 | 75% |
| Efficacy Supplements for New/Expanded Indications | 66 | 2 | 46 | 18 | 0 | 72% |
| All Original NDAs and BLAs | 124 | 3 | 76 | 42 | 3 | 64% |
| All Efficacy Supplements | 89 | 2 | 58 | 29 | 0 | 67% |

* Totals include applications with target dates that were inapplicable due to review of unsolicited amendments. These were not included in calculations of final performance.

The table below shows the number of times FDA met the target date because significant deficiencies in the application precluded discussion of labeling or PMRs/PMCs and FDA notified the applicant by the target date of this finding. It also shows the number of review timelines that were inapplicable due to FDA's decision to review solicited or unsolicited major amendments.

| Application Type | Met Target Date by Communicating Deficiencies | Target Date Inapplicable: Solicited Amendment | Target Date Inapplicable: Unsolicited Amendment |
|---|---|---|---|
| NMEs and BLAs | 6 | 1 | 0 |
| Efficacy Supplements for New/Expanded Indications | 3 | 0 | 2 |
| All Original NDAs and BLAs | 13 | 1 | 2 |
| All Efficacy Supplements | 3 | 0 | 2 |

### *Preliminary FY 2013 Cohort Performance*

Under PDUFA V, FDA is required to report performance in meeting the planned review timelines for all original NDAs and BLAs and all efficacy supplements. Some target dates were inapplicable due to FDA's receipt of a major amendment. A footnote to the table below provides specific information regarding three of the target dates that were met due to communicating application deficiencies to the applicant.

| Application Type | Number of 74-Day Letters With Timelines | Target Date Inapplicable | Target Date Met* | Target Date Not Met | Applications Pending within Target Date | Withdrawn | Percent of Applications Target Date Met |
|---|---|---|---|---|---|---|---|
| NDAs and BLAs | 110[†] | 5 | 24 | 13 | 66 | 1 | 65% |
| Efficacy Supplements | 67 | 2 | 22 | 14 | 28 | 1 | 61% |

* Target dates for two NDAs and one efficacy supplement were met due to communicating deficiencies.
[†] One NDA received a Complete Response action prior to the target date and is not reflected in the target performance, withdrawn, or pending columns.

## *Additional PDUFA V Commitments*

Section XIII of the PDUFA Commitment Letter pertains to reporting on FDA's progress on the additional program enhancements identified in the following sections of the Commitment Letter:

- Section IX: Enhancing Regulatory Science and Expediting Drug Development
- Section X: Enhancing Benefit-Risk Assessment in Regulatory Decision-Making
- Section XI: Enhancement and Modernization of the FDA Drug Safety System
- Section XII: Improving the Efficiency of Human Drug Review through Required Electronic Submissions and Standardization of Electronic Drug Application Data

These enhancements are designed to improve the efficiency of both drug development and the human drug review process. Section XIII specifies that this annual report must include descriptions of the hiring and placement of new staff and the use of PDUFA resources to complete this work. Like the rest of the federal government, FDA operated under partial sequestration in FY 2013, which included sequestration of FDA's user fees. The sequestered amount of PDUFA user fees approximated the PDUFA V increase that was agreed to with the regulated industry to complete these additional PDUFA V commitments. The PDUFA V increase could not be obligated during FY 2013. FDA accomplished the work described in the following tables with the staffing levels that were on board at the end of FY 2012. Any reference to increases in staff capacity noted in the tables below is attributable to the movement of existing staff to new roles. In future annual reports, FDA will report on the hiring and placement of new staff as the PDUFA user fee increase becomes available.

Section 104 of FDASIA further requires FDA to report on the agency's plans for meeting the PDUFA V commitments. At the beginning of PDUFA V, the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) convened a steering committee to oversee the implementation of PDUFA V. The committee is composed of key representatives from both Centers as well as the people responsible for implementing each PDUFA V enhancement. The committee meets approximately quarterly to review current progress and the plans for future work in each area to ensure timely completion of FDA's commitments.

The tables on the pages that follow describe FDA's progress in these areas. For more information on the PDUFA V enhancements, please see the PDUFA V Commitment Letter.[4]

[4] www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf

| Performance Goals | FY 2013 Accomplishments |
|---|---|
| **Enhancing Regulatory Science and Expediting Drug Development** | |
| **Promoting Innovation Through Enhanced Communication Between FDA and Sponsors During Drug Development** | • FDA established enhanced communication functions in CDER's Office of New Drugs and CBER's Manufacturer's Assistance and Technical Training Branch.<br>• FDA published a website[5] for sponsors to obtain more information about the role of enhanced communication and how sponsors should contact the respective Centers. |
| **Advancing the Science of Meta-Analysis Methodologies** | • FDA established a working group to plan for a public meeting on best practices in conducting meta-analyses to be held in the first quarter of FY 2014. |
| **Advancing the Use of Biomarkers and Pharmacogenomics** | • FDA established a working group that is planning a public meeting in FY 2014.<br>• FDA developed a 2-day continuing education program entitled *Clinical Genomics: Scientific and Regulatory Aspects* to train review staff. This will be held annually and recorded for new employees. |
| **Advancing Development of Patient-Reported Outcomes (PROs) and Other Endpoint Assessment Tools** | • FDA established a working group that is planning a public meeting in FY 2014.<br>• FDA organized a 2-day interactive course entitled *Introduction to the Science of Measurement and Application of Modern Measurement Theory to Improve Quality and Interpretability of Clinical Trial Data* on October 25-25, 2013, that was attended by approximately 75 FDA staff (e.g., medical officers, statisticians, etc.).<br>• FDA published a website[6] to provide a resource for sponsors to obtain more information about clinical outcome assessment development and qualification. |
| **Advancing Development of Drugs for Rare Diseases** | • FDA drafted a staffing and implementation plan for the Rare Disease Program in CDER's Office of New Drugs and increased the staff capacity of the Rare Disease Program to include the five positions stipulated in the Commitment Letter.<br>• FDA held a 2-day training on rare disease drug development on March 20-21, 2013, that was attended by over 100 FDA staff (e.g., medical officers, regulatory project managers). The training is expected to be an annual event with the next training planned for March 2014. |

[5] www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm327281.htm
[6] www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284077.htm

| Performance Goals | FY 2013 Accomplishments |
|---|---|
| **Enhancing Regulatory Science and Expediting Drug Development (continued)** | |
| **Advancing Development of Drugs for Rare Diseases (continued)** | • FDA also made progress in the following areas during FY 2013:<br>o Draft guidance on advancing and facilitating the development of drugs and biologics for rare diseases.<br>o Draft guidance on additional rare disease-related topics, such as natural history studies, formal meetings with FDA, and safety assessments.<br>o A public meeting on complex issues in clinical trials for rare disease drugs is scheduled for the second quarter of FY 2014.<br>• FDA completed construction of a database that will serve as an evaluation tool for the Rare Disease Program. |
| **Enhancing Benefit-Risk Assessment in Regulatory Decision-Making** | |
| **Implementation of a Structured Framework for Benefit-Risk Assessment in the New Drug and Biologic Review Process** | • In March 2013, FDA published an implementation plan for a structured approach to benefit-risk assessment in drug review.<br>• FDA established working groups in both CDER and CBER to integrate a benefit-risk framework into each Center's clinical review template. |
| **Patient-Focused Drug Development (PFDD)** | • FDA convened an initial public meeting in October 2012 to obtain public input on the disease areas that should be addressed in PFDD meetings during FY 2013 - 2015.<br>• FDA convened a series of consultation meetings with patient advocacy groups to address key considerations and challenges in establishing a process for conducting the PFDD meetings that will be useful to both the patient community and FDA.<br>• FDA published a list of 16 disease areas that will be addressed in PFDD meetings during FY 2013 – 2015.<br>• FDA held four PFDD meetings during FY 2013 on myalgic encephalomyelitis/chronic fatigue syndrome, human immunodeficiency virus, lung cancer, and narcolepsy.<br>• In September 2013, FDA published the summary report of the April 2013 meeting on myalgic encephalomyelitis/chronic fatigue syndrome. |
| **Enhancement and Modernization of the FDA Drug Safety System** | |
| **Measure the Effectiveness of Risk Evaluation and Mitigation Strategy (REMS) and Standardize and Better Integrate REMS into the Healthcare System** | • FDA convened a working group to develop a draft guidance regarding the determination that FDA makes on whether or not a REMS is necessary.<br>• FDA convened a working group to develop a draft guidance on evidence based methodologies for evaluating the effectiveness and burden of REMS.<br>• FDA held a public meeting on July 25-26, 2013, to obtain input on issues and challenges associated with the standardization and assessment of REMS for drug and biological products.<br>• FDA began drafting a report to identify priority projects and workplans in the areas of pharmacy systems, prescriber education, providing benefit-risk information to patients, and practice settings. |

| Performance Goals | FY 2013 Accomplishments |
|---|---|
| **Enhancement and Modernization of the FDA Drug Safety System (continued)** | |
| **Sentinel as a Tool for Evaluating Drug Safety Issues That May Require Regulatory Action** | • FDA planned for a public workshop scheduled in the second quarter of FY 2014 to discuss a variety of topics on active medical product surveillance, including current and emerging Sentinel projects as well as projects that would be appropriate to determine the feasibility of using Sentinel to evaluate drug safety issues that may require regulatory action.<br>• FDA is currently funding multiple medical product assessments/studies and methodological development studies to further evaluate the utility and validity of Sentinel. |
| **Conduct and Support Activities Designed to Modernize the Process of Pharmacovigilance** | • FDA formed the FDA Adverse Event Reporting System (FAERS) Data Quality Working Group to address data quality issues generated from the migration of the former adverse event reporting system to FAERS and with data capture in FAERS.<br>• FAERS data entry initiated an optical character recognition and machine learning pilot program to evaluate this technology as a means of expediting data entry processes.<br>• FDA began drafting CDER-specific requirements and guidance for acceptance of individual case safety reports using the Efficacy Topics' Data Elements for Transmission of Adverse Drug Reactions Reports (E2B(R3)) data standard adopted by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).<br>• FDA is developing requirements to use the Safety Reporting Portal as a means for smaller pharmaceutical manufacturers to submit adverse event reports in a non-E2B format, in preparation of the pending Electronic Reporting Rule.<br>• FDA created and maintains the FAERS Manufacturer Dictionary, a repository of collected and indexed manufacturer names, synonyms, and related information, used by MedWatch Coders to match and validate reported firm names.<br>• FDA created and maintains the FAERS Product Dictionary, a listing of FDA-regulated products and product information used by FDA for validating, mapping, and coding suspect medical products listed in FAERS adverse event reports.<br>• FDA participates in ICH and Council for International Organizations of Medical Sciences Medical Dictionary for Regulatory Activities (MedDRA) workgroups as well as ongoing internal MedDRA upversioning, coding, and training efforts. |

| Performance Goals | FY 2013 Accomplishments |
|---|---|
| **Enhancement and Modernization of the FDA Drug Safety System (continued)** | |
| **Information Systems and Infrastructure** | • FDA completed user acceptance training for release 2.2.3 for FAERS in September 2013.<br>• In March 2013, FDA updated MedDRA and desktop browser to version 16.0.<br>• In June 2013, FDA completed the FAERS Business Intelligence Solution (FBIS) platform and database upgrade to Oracle 11g/Exadata platform.<br>• In June 2013, FDA performed data refresh in FBIS pre-production environment.<br>• FDA implemented the ability to archive the results of Sentinel analyses.<br>• CBER is currently in the process of developing guidance for electronic submission of Lot Distribution Data. CBER is also working to develop the capability to receive manufacturer Vaccine Adverse Event Reporting System reports electronically.<br>• FDA introduced a business process system that supports work process management. |
| **Improving the Efficiency of Human Drug Review Through Required Electronic Submissions and Standardization of Electronic Drug Application Data** | |
| **Electronic Submissions Requirement** | • FDA published a draft guidance to industry on providing regulatory submissions in electronic format using Electronic Common Technical Document specifications. |
| **Standardization of Drug Application Data** | • In September 2013, FDA published for public comment a project plan that describes FDA's Therapeutic Area Standards Initiative.<br>• FDA collaborated with academia, regulated industry, and standards development organizations to develop therapeutic/disease area data standards.<br>• Throughout FY 2013, FDA began drafting a series of guidances that will specify electronic study data standards, formats, and terminologies for the regulated industry. |

| Performance Goals | FY 2013 Accomplishments |
|---|---|
| **Information Technology Goals** | |
| **Communications and Technical Interactions** | • Meetings with FDA and industry were conducted quarterly and occurred on the following dates: October 26, 2012, January 13, 2013, May 2, 2013, and September 12, 2013. All meetings discussed the implementation of the plan, identified opportunities for continual quality improvement, made modifications to the plan when appropriate, and assessed potential impacts among FDA and stakeholders.<br>• The PDUFA V IT Plan summary was presented at the September 12, 2013, PDUFA Industry Meeting.<br>• FDA incorporated feedback received from industry that clarified the pharmaceutical industry's expectations and provided recommendations for FDA to consider as the PDUFA IT Plan was developed.<br>• The PDUFA V Information Technology Plan Draft has been approved by FDA management and will be published for industry comment by the end of the second quarter of FY 2014.<br>• The annual assessment is in progress and is expected to be published for industry comment by the end of the second quarter of FY 2014. |
| **Metrics and Measures** | • FDA has tracked and reported its progress for the required metrics, which will be reported in the PDUFA IT Annual Assessment, and published for industry comment no later than December 31, 2013.<br>• FDA will report its financial metrics in the PDUFA Financial Reports, submitted to Congress each fiscal year on PDUFA program activities, collections, and spending. |

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# *Appendices*

## Appendix A: Final FY 2012 Cohort Performance Detail

The following tables detail the final performance for the FY 2012 cohort of submissions. These data include the number of submissions reviewed *on time* (acted on by the PDUFA goal date) or *overdue* (acted on past goal or pending past the goal date) and the final *percent on time* (final performance with no actions pending within the PDUFA goal date). The performance data presented here have been updated from the preliminary performance information reported in the FY 2012 PDUFA Performance Report.

### Review Goal Performance

#### Original Applications

| Original Application Type | Performance Goal | Filed | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Priority NMEs and BLAs | Act on 90 percent within 6 months | 18 | 17 | 1 | 94% |
| Standard NMEs and BLAs | Act on 90 percent within 10 months | 32 | 32 | 0 | 100% |
| Priority NDAs and BLAs | Act on 90 percent within 6 months | 26 | 25 | 1 | 96% |
| Standard NDAs and BLAs | Act on 90 percent within 10 months | 104 | 101 | 3 | 97% |

#### Resubmitted Applications

| Resubmitted Application Type | Performance Goal | Received | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Class 1 | Act on 90 percent within 2 months | 6 | 6 | 0 | 100% |
| Class 2 | Act on 90 percent within 6 months | 36 | 36 | 0 | 100% |

#### Efficacy Supplements

| Efficacy Supplement Type | Performance Goal | Filed | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Priority | Act on 90 percent within 6 months | 39 | 39 | 0 | 100% |
| Standard | Act on 90 percent within 10 months | 108 | 105 | 3 | 97% |

### Resubmitted Efficacy Supplements

| Resubmitted Efficacy Supplement Type | Performance Goal | Received | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Class 1 | Act on 90 percent within 2 months | 4 | 4 | 0 | 100% |
| Class 2 | Act on 90 percent within 6 months | 19 | 16 | 3 | 84% |

### Manufacturing Supplements

| Manufacturing Supplement Type | Performance Goal | Filed | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Prior Approval Required | Act on 90 percent within 4 months | 872 | 811 | 61 | 93% |
| Prior Approval Not Required | Act on 90 percent within 6 months | 1,566 | 1,476 | 90 | 94% |

## Procedural and Processing Goal Performance

### Meeting Management

| Type | Performance Goal | Received* | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Type A Meeting Requests | Review 90 percent within 14 days | 184 | 156 | 28 | 85% |
| Type B Meeting Requests | Review 90 percent within 21 days | 1,322 | 1,126 | 196 | 85% |
| Type C Meeting Requests | Review 90 percent within 21 days | 785 | 682 | 103 | 87% |
| Type A Meetings Scheduled | Review 90 percent within 30 days | 168 | 158 | 10 | 94% |
| Type B Meetings Scheduled | Review 90 percent within 60 days | 1,261 | 1,176 | 85 | 93% |
| Type C Meetings Scheduled | Review 90 percent within 75 days | 725 | 662 | 63 | 91% |
| Meeting Minutes | Review 90 percent within 30 days | 1,585 | 1,351 | 234 | 85% |

* Not all meeting requests are granted; therefore, the number of meetings scheduled may differ from the number of meeting requests received. Not all scheduled meetings are held; therefore, the number of meeting minutes may differ from the number of meetings scheduled.

### Major Dispute Resolutions

| Performance Goal | Responses* | On Time | Overdue | Percent On Time |
|---|---|---|---|---|
| Respond to 90 percent within 30 days | 32 | 31 | 1 | 97% |

* This figure represents the number of FDA-generated 30-day responses to requests for review that have been received. It is not representative of the number of unique appeals received that have been reviewed, as there may be more than one response to an original appeal.

### Responses to Clinical Holds

| Performance Goal | Received | On Time | Overdue | Percent On Time |
|---|---|---|---|---|
| Respond to 90 percent within 30 days | 178 | 157 | 21 | 88% |

### Special Protocol Assessments

| Performance Goal | Received | On Time | Overdue | Percent On Time |
|---|---|---|---|---|
| Respond to 90 percent within 45 days | 288 | 259 | 29 | 90% |

### Special Protocol Assessments – FY 2012 Resubmissions

| Total Resubmissions | Applications with 1 Resubmission | Applications with 2 Resubmissions | Applications with 3 Resubmissions |
|---|---|---|---|
| 54 | 41 | 5 | 1 |

### Drug/Biological Product Proprietary Names

| Submission Type | Performance Goal | Received | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| Submitted During IND Phase | Review 90 percent within 180 days | 164 | 163 | 1 | 99% |
| Submitted with NDA/BLA | Review 90 percent within 90 days | 216 | 213 | 3 | 99% |

### First-Cycle Filing Review Notifications

| Notification Type | Performance Goal | Filed | On Time | Overdue | Percent On Time |
|---|---|---|---|---|---|
| NDAs and BLAs | Act on 90 percent within 74 days | 126 | 122 | 4 | 97% |
| Efficacy Supplements | Act on 90 percent within 74 days | 96 | 90 | 6 | 94% |

## Notification of Planned Review Timelines

| Application Type | Applications Filed* | In 74-Day Letter | Not In 74-Day Letter | Percent In 74-Day Letters |
|---|---|---|---|---|
| Original NMEs and BLAs | 48 | 46 | 2 | 96% |
| All Original NDAs and BLAs | 126 | 124 | 2 | 98% |
| Efficacy Supplements for New/Expanded Indications | 72 | 66 | 5 | 93%† |
| All Efficacy Supplements | 96 | 89 | 5 | 95%† |

* The number of original applications filed in any given year may not match the number of first-cycle notifications due to the status of an application at the time the data are reported.

† Two efficacy supplement applications (including one for a new/expanded indication) were never issued 74-day letters and were not included in calculations of final performance.

# Appendix B: Preliminary FY 2013 Cohort Performance Detail

The following detailed performance information for FY 2013 cohort submissions includes the number of submissions filed, reviewed *on time* (acted on by the PDUFA goal date), and *overdue* (acted on past goal or pending past the goal date). The number of submissions not yet acted on, but still pending within the PDUFA goal date (*pending within goal*) is also provided, along with the highest possible percent of reviews that may be completed on time.

## Review Goal Performance

### Products Reviewed Under New PDUFA V Review Program

The table below represents NME NDAs and original BLAs that were reviewed under the PDUFA V NME NDA and Original BLA Review Program. Applications that were received as NME NDAs may not retain that status upon final action or approval. For example, this can occur when an applicant submits two separate applications for the same NME at the same time or while the first application is still under review. Both applications would be reviewed under the Program, though upon approval of either application as an NME, the second one would no longer be considered an NME. However, since both applications were reviewed under the Program, they are included in this table for Program analysis. In addition, although the Program only applies to NME NDAs and original BLAs, there is the potential that when there are multiple applications for the same NME, the second NME application could convert to an efficacy supplement upon approval of the first NME application. Because these applications would be reviewed under the Program, they are included as efficacy supplements in the table below. Furthermore, some applications that were submitted as original BLAs under existing FDA guidance may not be considered novel products to which the Program is targeted. In such cases, these original BLAs were not reviewed in the Program. For the reasons described in this paragraph, the figures in the table below may differ from the figures provided under the original application counts used for performance goal tracking elsewhere in this report.

| Application Type (Final Designation) | Performance Goal: Act on 90 percent within | Filed | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Priority NDAs and BLAs | 6 months of filing date | 19 | 3 | 0 | 16 | 100% | 100% |
| Standard NDAs and BLAs | 10 months of filing date | 35 | 3 | 0 | 32 | 100% | 100% |
| NDAs and BLAs Review Priority Undesignated* | To Be Determined | 0 | -- | -- | -- | -- | -- |
| Priority Efficacy Supplements† | 6 months of filing date | 0 | -- | -- | -- | -- | -- |
| Standard Efficacy Supplements† | 10 months of filing date | 0 | -- | -- | -- | -- | -- |
| Efficacy Supplements Review Priority Undesignated* | To Be Determined | 0 | -- | -- | -- | -- | -- |
| **Total Program Performance** | **--** | **54** | **6** | **0** | **48** | **100%** | **100%** |

*These applications have not reached the 60-day filing date and have not yet received a review priority designation.
† Some applications that are submitted as NME NDAs may be considered efficacy supplements at the time of approval.

## Original Applications

| Original Application Type | Performance Goal: Act on 90 percent within | Filed | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Priority NMEs & BLAs | 6 months of filing date | 19 | 3 | 0 | 16 | 100% | 100% |
| Standard NMEs & BLAs | 10 months of filing date | 36 | 3 | 0 | 33 | 100% | 100% |
| Priority Non-NME NDAs* | 6 months | 9 | 1 | 0 | 8 | 100% | 100% |
| Standard Non-NME NDAs* | 10 months | 72 | 7 | 0 | 65 | 100% | 100% |
| Review Priority Undesignated† | To Be Determined | 0 | -- | -- | -- | -- | -- |

* Starting in FY 2013, under PDUFA V, FDA is required to report non-NME NDAs separately (instead of all NDAs and BLAs as reported in previous years).
† These applications have not reached the 60-day filing date and have not yet received a review priority designation.

## Resubmitted Applications

| Resubmitted Application Type | Performance Goal: Act on 90 percent within | Received | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Class 1 | 2 months | 11 | 11 | 0 | 0 | 100% | 100% |
| Class 2 | 6 months | 40 | 20 | 0 | 20 | 100% | 100% |

## Efficacy Supplements

| Efficacy Supplement Type | Performance Goal: Act on 90 percent within | Filed | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Priority | 6 months | 27 | 12 | 0 | 15 | 100% | 100% |
| Standard | 10 months | 112 | 22 | 3 | 87 | 88% | 97% |
| Review Priority Undesignated† | To Be Determined | 3 | -- | -- | -- | -- | -- |

† These applications have not reached the 60-day filing date and have not yet received a review priority designation.

## Resubmitted Efficacy Supplements

| Resubmitted Efficacy Supplement Type | Performance Goal: Act on 90 percent within | Received | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Class 1 | 2 months | 2 | 2 | 0 | 0 | 100% | 100% |
| Class 2 | 6 months | 9 | 5 | 1 | 3 | 83% | 89% |

### Manufacturing Supplements

| Manufacturing Supplement Type | Performance Goal: Acton 90 percent within | Filed | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Prior Approval Required | 4 months | 865 | 553 | 47 | 265 | 92% | 95% |
| Prior Approval Not Required | 6 months | 1,521 | 841 | 31 | 649 | 96% | 98% |
| Review Priority Undesignated† | To Be Determined | 2 | -- | -- | -- | -- | -- |

† These applications have not reached the 60-day filing date and have not yet received a review priority designation.

## Procedural and Processing Goal Performance

### Meeting Management

| Type | Performance Goal: Review 90 percent within | Received* | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Type A Meeting Requests† | 14 Days | 188 | 123 | 23 | 42 | 84% | 88% |
| Type B Meeting Requests | 21 Days | 1,370 | 1,203 | 144 | 23 | 89% | 89% |
| Type C Meeting Requests | 21 Days | 888 | 757 | 113 | 18 | 87% | 87% |
| Type A Meetings Scheduled† | 30 Days | 170 | 106 | 15 | 49 | 88% | 91% |
| Type B Meetings Scheduled | 60 Days | 1,176 | 1,024 | 92 | 60 | 92% | 92% |
| Type C Meetings Scheduled | 75 Days | 593 | 502 | 43 | 48 | 92% | 93% |
| Type B Written Response | 60 Days | 148 | 86 | 38 | 24 | 69% | 74% |
| Type C Written Response | 75 Days | 251 | 152 | 43 | 56 | 78% | 83% |
| Meeting Minutes | 30 Days | 1,418 | 938 | 129 | 351 | 88% | 91% |

* Not all meeting requests are granted; therefore, the number of meetings scheduled may differ from the number of meeting requests received. Not all scheduled meetings are held; therefore, the number of meeting minutes may differ from the number of meetings scheduled.

† Some meeting requests and subsequent scheduling of meetings are for requests where the type cannot be initially determined. There were 105 meetings (54 requests and 51 schedulings) coded as undesignated in the database as of September 30, 2013. These undesignated meetings are included as Type A meetings in the table above. Performance in all categories will change once designations are made for these requests and schedulings and will be updated in the FY 2014 PDUFA Performance Report.

### Major Dispute Resolutions

| Performance Goal | Responses* | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|
| Respond to 90 percent within 30 days | 29 | 21 | 0 | 8 | 100% | 100% |

* This figure represents the number of FDA-generated 30-day responses to requests for review that have been received. It is not representative of the number of unique appeals received that have been reviewed, as there may be more than one response to an original appeal.

### Responses to Clinical Holds

| Performance Goal | Received | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|
| Respond to 90 percent within 30 days | 162 | 136 | 18 | 8 | 88% | 89% |

### Special Protocol Assessments

| Performance Goal | Received | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|
| Respond to 90 percent within 45 days | 220 | 185 | 13 | 22 | 93% | 94% |

### Special Protocol Assessments – FY 2013 Resubmissions

| Total Resubmissions | Applications with 1 Resubmission | Applications with 2 Resubmissions | Applications with 3 Resubmissions |
|---|---|---|---|
| 40 | 28 | 6 | 0 |

### Drug/Biological Product Proprietary Names

| Submission Type | Performance Goal: Review 90 percent within | Received | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| Proprietary Names Submitted During IND Phase | 180 days | 157 | 95 | 4 | 58 | 96% | 97% |
| Proprietary Names Submitted with NDA/BLA | 90 days | 235 | 201 | 5 | 29 | 98% | 98% |

### First-Cycle Filing Review Notifications

| First-Cycle Filing Review Notification Type | Performance Goal: Act on 90 percent within | Filed | On Time | Overdue | Pending Within Goal | Current Percent On Time | Highest Possible Percent On Time |
|---|---|---|---|---|---|---|---|
| NDAs and BLAs | 74 days | 136 | 100 | 2 | 34 | 98% | 99% |
| Efficacy Supplements | 74 days | 93 | 66 | 8 | 19 | 89% | 91% |

### Notification of Planned Review Timelines

| Application Type* | Applications Filed† | In 74-Day Letter | Not In-74 Day Letter | Pending‡ | Percent In 74-Day Letters | Highest Possible Percent In Letters |
|---|---|---|---|---|---|---|
| NDAs and BLAs | 136 | 110 | 0 | 26 | 100% | 100% |
| Efficacy Supplements | 93 | 67 | 4 | 22 | 94% | 96% |

* Under PDUFA V, FDA is required to report on planned review timeline notification performance only for NDAs and BLAs and efficacy supplements.
† The number of original applications filed in any given year may not match the number of first-cycle notifications due to the status of an application at the time the data are reported. Numbers are updated as appropriate in later fiscal year reports.
‡ Pending includes only those notification commitments that have not been issued and are within 74 days.

## Additional PDUFA V Review Program Reporting

### Program Quality Metrics

The table below provides information on review activity for applications reviewed and acted on under the Program. The data presented in the table below represent the six applications that were received and acted on during FY 2013. Two of the six applications were withdrawn during FDA review. The review activity of remaining applications that were received in FY 2013 will be reported in future reports once those applications have received an FDA action.

| Quality System Metric | FY 2013 |
|---|---|
| Applications Filed with a First Action in FY 2013 | 6 |
| Pre-NDA/BLA Meetings Held | 6 |
| Applications with Agreement on Complete Application | 5 |
| Applications with Agreement on Late Component Submission | 5 |
| 74-Day Letters Issued | 6 |
| Mid-Cycle Communications | 6 |
| Primary Reviews Completed | 34 |
| Secondary Reviews Completed | 33 |
| Late Cycle Meeting Packages | 4 |
| Late Cycle Meetings Held | 4 |
| Discipline Review Letters Issued | 2 |
| *Disciplines Referenced in Discipline Review Letters* | |
| Clinical | 1 |
| Clinical Pham | 1 |
| Nonclinical | 1 |
| Quality | 2 |
| Statistical | 1 |

**Independent Assessment of the Program**

To understand the Program's impact on NME NDA and original BLA reviews, FDA committed in the PDUFA V Commitment Letter to contract with an independent firm to evaluate the Program. Two assessments of the Program will be published during PDUFA V: an interim assessment by March 31, 2015, and a final assessment by December 31, 2016. Before beginning PDUFA V, FDA published a statement of work for the independent assessment and awarded this work to Eastern Research Group, Inc. (ERG). Section 104 of FDASIA further requires FDA to report on the status of the independent assessment of the Program in the annual PDUFA performance report.

The Program's goal is to improve the efficiency and effectiveness of the first-cycle review process through increased transparency and communication. The Program elements that allow for this include mid-cycle communications and late-cycle meetings between the applicant and review team, briefing packages sent prior to late-cycle meetings outlining substantive review issues, and specific agreements on the contents of a complete application that may be reached at a pre-submission meeting. To ensure a comprehensive evaluation, ERG is responsible for evaluating each interaction between FDA and an applicant by examining FDA and applicant documents and by analyzing events in the review process as they occur or soon thereafter. After FDA takes action on a Program application, ERG also conducts interviews with the applicant and the FDA review team to identify best practices and opportunities for improvement of the Program. As stated earlier in this report, FDA received a total of 54 applications (33 NME NDAs and 21 BLAs) for review in the Program in FY 2013. Four applications were approved, two were withdrawn after filing by the applicant, and two applications received a refuse-to-file action. The remaining applications were still pending FDA first action at the end of FY 2013.

By the end of FY 2013, ERG had evaluated numerous interactions between FDA and applicants, including 44 pre-submission meetings, 33 mid-cycle communications, and 17 late-cycle meetings. For the applications that received a first-cycle FDA action by September 30, 2013, ERG also conducted post-action interviews with the applicants and the FDA review teams. To date, these evaluations indicate that the Program is being implemented as agreed between FDA and industry in the PDUFA V Commitment Letter.

# Appendix C: List of Approved Applications

This appendix includes the detailed review histories of the NDA and BLA submissions approved under PDUFA V in FY 2013. Approvals are grouped by priority designation and submission year and listed in order of total approval time. Approval time is presented in months and includes each review cycle's time with FDA, time with the sponsor, and the total time on that application.

Review histories of NDA and BLA submissions approved prior to FY 2013 can be found in the appendices of the earlier PDUFA Performance Reports available at: www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/default.htm.

**Please note:** When determining total time, FDA calculates the number of months and rounds to the nearest tenth. However, when cycle times are added, rounding discrepancies can occur. That is, the rounding of individual cycles and applicant times to the nearest tenth can, in some cases, result in times that, when added, may not appear to add correctly (differing by 0.1 month). For example on page C-3, the submission *Flublok (influenza vaccine)* had a rounded total time of 4.4 months after the first cycle, followed by a rounded applicant time of 8.0 months. Adding these times together suggests that the total time should then be 12.4 months; however, the actual rounded total time after the third cycle and applicant review was 12.3 months.

Because months consist of varying numbers of days, FDA uses the average number of days in a month to calculate review time in months. Therefore, a submission may appear overdue even though it was approved on the goal date. For example, the submission Cometriq (cabozantinib) on page C-2 was received on May 29, 2012, and had a 6-month review goal date of November 29, 2012. FDA approved the submission on the goal date, but because FDA uses the average number of days in a month to calculate months, the time taken to review the submission is reported as 6.1 months and the review appears overdue. Cycles with this type of rounding inconsistency are footnoted in the tables that follow.

## Terms and Coding Used in Tables

BLAs are indicated in italics.

Action Codes: AE = Approvable
AP = Approved
CR = Complete Response
NA = Not Approvable
TA = Tentative Approval
WD = Withdrawn

◊ Expedited review and TA of an NDA by FDA for fixed dose combinations and co-packaged antiretroviral medications as part of the President's Emergency Plan for AIDS Relief (PEPFAR)

+ Major amendment was received, which extended the action goal date by 3 months [Note: Under PDUFA V, a major amendment can be received anytime during the review cycle and extend the goal date by 3 months. If the review cycle occurred prior to FY 2013, the major amendment must have been received within 3 months of the action due date to extend the action goal date by 3 months.]

▲ Denotes Class 1 Resubmission (2 month review-time goal)

△ Denotes Class 2 Resubmission (6 month review-time goal)

## Table 1
## FY 2013 Priority NDA and BLA Approvals (by FY of receipt)

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2013*** | | | | | | | |
| Xofigo (radium Ra 223 dichloride) | Bayer Healthcare Pharmaceuticals, Inc. | Y | First | 5.0 | AP | 5.0 | Y[7] |
| Tivicay (dolutegravir) | Viiv Healthcare Co | Y | First | 7.8 | AP | 7.8 | Y[6] |
| Gilotrif (afatinib) | Boehringer Ingelheim | Y | First | 7.9 | AP | 7.9 | Y[6] |
| ***Submitted in FY 2012*** | | | | | | | |
| Iclusig (ponatinib) | Ariad Pharmaceuticals, Inc. | Y | First | 2.6 | AP | 2.6 | Y |
| *Varizig (varicella zoster immune globulin)* | *Cangene Corporation* | Y | First | 5.7 | AP | 5.7 | Y |
| Aciphex Sprinkle (*rabeprazole sodium)* | Eisai, Inc. | N | First | 5.9 | AP | 5.9 | Y |
| *Kadcyla (trastuzumab emtansine)* | *Genentech, Inc.* | Y | First | 5.9 | AP | 5.9 | Y |
| *Jetrea (ocriplasmin)* | *Thrombogenics Inc.* | Y | First | 6.0 | AP | 6.0 | Y |
| Efavirenz, Lamivudine, Tenofovir disoproxil fumarate Tablets, 600 Mg/300 Mg/300 Mg | Hetero Labs Ltd | N | First | 6.0 | TA | 6.0 | Y◊ |
| Sirturo (bedaquiline) | Janssen Therapeutics Div Janssen Products LP | Y | First | 6.0 | AP | 6.0 | Y |
| Dotarem (gadoterate meglumine) | Guerbet LLC | Y | First | 6.0 | AP | 6.0 | Y |
| (phenylephrine hydrochloride) | Paragon Bioteck Inc | N | First | 6.0 | AP | 6.0 | Y |
| Cometriq (cabozantinib) | Exelixis Inc | Y | First | 6.1 | AP | 6.1 | Y* |
| Delzicol (mesalamine) Delayed-Release Capsules | Warner Chilcott Co LLC | N | First | 6.1 | AP | 6.1 | Y* |
| *BAT (botulism antitoxin heptavalent - equine)* | *Cangene Corporation* | Y | First | 6.1 | AP | 6.1 | Y* |
| Fulyzaq (Crofelemer) | Salix Pharmaceuticals, Inc. | Y | First | 12.9 | AP | 12.9 | N+ |
| Nymalize (nimodipine) | Arbor Pharmaceuticals, Inc. | N | First | 9.0 | CR | 9.0 | Y+ |
| | | | Sponsor | 3.2 | -- | 12.2 | -- |
| | | | Second | 5.6 | AP | 17.8 | Y△ |

* These submissions met the review goal, but due to rounding, they appear overdue.

[7] These applications are Program NMEs with review-time goals of 6 months from the 60-day filing date, giving them each an 8-month total review-time goal.

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2011*** | | | | | | | |
| Eliquis (apixaban) | Bristol Myers Squibb Co Pharmaceutical Research Institute | Y | First | 8.8 | CR | 8.8 | Y+ |
| | | | Sponsor | 2.9 | -- | 11.7 | -- |
| | | | Second | 3.4 | AP | 15.1 | Y△ |
| ***Submitted in FY 2010*** | | | | | | | |
| Cystaran (cysteamine) | Sigma Tau Pharmaceuticals Inc | N | First | 6.0 | CR | 6.0 | Y |
| | | | Sponsor | 19.0 | -- | 25.0 | -- |
| | | | Second | 6.0 | AP | 31.0 | Y△ |
| ***Submitted in FY 2009*** | | | | | | | |
| *(raxibacumab)* | *Human Genome Sciences, Inc.* | Y | First | 6.0 | CR | 6.0 | Y |
| | | | Sponsor | 31.0 | -- | 37.1 | -- |
| | | | Second | 6.0 | AP | 43.1 | Y△ |
| ***Submitted in FY 2008*** | | | | | | | |
| *Flublok (influenza vaccine)* | *Protein Sciences Corporation* | Y | First | 4.4 | CR | 4.4 | Y |
| | | | Sponsor | 8.0 | -- | 12.3 | -- |
| | | | Second | 8.5 | CR | 20.8 | Y△+ |
| | | | Sponsor | 30.2 | -- | 51.0 | -- |
| | | | Third | 6.0 | AP | 56.9 | Y△ |

## Table 2
## FY 2013 Standard NDA and BLA Approvals (by FY of receipt)

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2013*** | | | | | | | |
| Vogelxo (testosterone) | Upsher Smith Laboratories, Inc. | N | First | 9.9 | TA | 9.9 | Y |
| Mirvaso (brimonidine tartrate) | Galderma Research and Development, Inc. | N | First | 9.9 | AP | 9.9 | Y |
| Brintellix (vortioxetine) | Takeda Pharmaceuticals USA Inc | Y | First | 11.9 | AP | 11.9 | Y[8] |
| ***Submitted in FY 2012*** | | | | | | | |
| Synribo (omacetaxine mepesuccinate) | Ivax International Gmbh | Y | First | 6.9 | AP | 6.9 | Y |
| adrenalin (epinephrine injection) | JHP Pharmaceuticals LLC | N | First | 9.1 | AP | 9.1 | Y |
| Onfi (clobazam) | Lundbeck LLC | N | First | 9.6 | AP | 9.6 | Y |
| Juxtapid (lomitapide Mesylate) | Aegerion Pharmaceuticals, Inc. | Y | First | 9.8 | AP | 9.8 | Y |
| Lo Minastrin Fe (norethindroneacetate and ethinyl estradiol chewable tablets, ethinyl estradiol chewable tablets and ferrous fumarate tablets) | Warner Chilcott Co LLC | N | First | 9.8 | AP | 9.8 | Y |
| Mekinist (trametinib) | Glaxosmithkline LLC | Y | First | 9.8 | AP | 9.8 | Y |
| *Rixubis (coagulation factor IX, recombinant)* | *Baxter Healthcare Corporation* | Y | First | 9.9 | AP | 9.9 | Y |
| Khedezla (desvenlafaxine) | Osmotica Pharmaceutical Corp | N | First | 9.9 | AP | 9.9 | Y |
| Minastrin 24 Fe (norethindrone acetate and ethinyl estradiol soft gelatin capsules, and ferrous fumarate tablets) | Warner Chilcott Co, Inc. | N | First | 9.9 | AP | 9.9 | Y |
| Invokana (canagliflozin) | Janssen Pharmaceuticals, Inc. | Y | First | 9.9 | AP | 9.9 | Y |
| Quartette (levonorgestrel/ethinyl estradiol and ethinyl estradiol) | Teva Branded Pharmaceutical Products R And D, Inc. | N | First | 9.9 | AP | 9.9 | Y |
| Astagraf Xl (tacrolimus extended-release capsules) | Astellas Pharma US, Inc. | N | First | 9.9 | AP | 9.9 | Y |
| Zubsolv (buprenorphine And naloxone sublingual tablets) | Orexo Ab | N | First | 9.9 | AP | 9.9 | Y |

[8] This application is a Program NME with a review-time goal of 10 months from the 60-day filing date, giving it a 12-month total review-time goal.

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2012*** | | | | | | | |
| Breo Ellipta (fluticasone furoate/vilanterol inhalation powder ) | Glaxo Group Ltd England DBA Glaxosmithkline | Y | First | 9.9 | AP | 9.9 | Y |
| Signifor (pasireotide) | Novartis Pharmaceuticals Corp | Y | First | 9.9 | AP | 9.9 | Y |
| Naftin (naftifine hydrochloride) | Merz Pharmaceuticals LLC | N | First | 9.9 | AP | 9.9 | Y |
| *Simponi Aria (golimumab)* | *Janssen Biotech, Inc.* | N | First | 10.0 | AP | 10.0 | Y |
| Fetzima (levomilnacipran) | Forest Laboratories, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Simbrinza (brinzolamide/ brimonidine tartrate opthalmic suspension) | Alcon Research Ltd | N | First | 10.0 | AP | 10.0 | Y |
| Vituz (hydrocodone bitartrate and chlorpheniramine maleate) | Cypress Pharmaceutical, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Bloxiverz (neostigmine methylsulfate) | Eclat Pharmaceuticals LLC | N | First | 10.0 | AP | 10.0 | Y |
| Topicort (desoximetasone) | Taro Pharmaceuticals USA, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Brisdelle (paroxetine) | Noven Therapeutics LLC | N | First | 10.0 | AP | 10.0 | Y |
| Diclegis (doxylamine succinate/pyridoxine hydrochloride) | Duchesnay, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Efavirenz, Lamivudine, Tenofovir disoproxil fumarate tablets, 600 mg/300 mg/300 mg | Aurobindo Pharma Ltd | N | First | 10.0 | TA | 10.0 | Y◊ |
| Oxytrol For Women (oxybutynin Transdermal System) | MSD Consumer Care, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Tafinlar (dabrafenib) | Glaxosmithkline | Y | First | 10.0 | AP | 10.0 | Y |
| Fycompa (perampanel) | Eisai, Inc. | Y | First | 10.0 | AP | 10.0 | Y |
| (palonosetron hydrochloride) | Dr Reddys Laboratories Ltd | N | First | 10.0 | TA | 10.0 | Y |
| Lamivudine/ Nevirapine/ Zidovudine FDC Scored Tablets For Oral Suspension, 30mg/50mg/60mg | Cipla Ltd | N | First | 10.0 | TA | 10.0 | Y◊ |
| Prolensa (bromfenac ophthalmic solution) | Bausch And Lomb, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| (norethindrone acetate and ethinyl estradiol chewable tablets, and ferrous fumarate tablets) | Warner Chilcott Co LLC | N | First | 10.0 | AP | 10.0 | Y |

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2012*** | | | | | | | |
| (leuprolide acetate for depot suspension and norethindrone acetate tablets) | Abbvie Endocrine, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Minivelle (estradiol) | Noven Pharmaceuticals, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Nucynta (tapentadol) | Janssen Pharmaceuticals, Inc. | N | First | 10.0 | AP | 10.0 | Y |
| Daptomycin | Hospira, Inc. | N | First | 10.0 | TA | 10.0 | Y |
| Pomalyst (pomalidomide) | Celgene Corp | Y | First | 10.0 | AP | 10.0 | Y |
| (aspirin) | PLX Pharma, Inc. | N | First | 10.1 | AP | 10.1 | Y* |
| Kynamro (mipomersen sodium) | Genzyme Corp | Y | First | 10.1 | AP | 10.1 | Y* |
| Oxtellar XR (oxcarbazepine) | Supernus Pharmaceuticals, Inc. | N | First | 10.1 | AP | 10.1 | Y* |
| Ilevro (nepafenac) | Alcon Research Ltd | N | First | 10.1 | AP | 10.1 | Y* |
| Osphena (ospemifene) | Shionogi, Inc. | Y | First | 10.1 | AP | 10.1 | Y* |
| (phenylephrine hydrochloride injection, USP) | West Ward Pharmaceutical Corp | N | First | 9.9 | CR | 9.9 | Y |
| | | | Sponsor | 0.7 | -- | 10.6 | -- |
| | | | Second | 0.7 | AP | 11.3 | Y▲ |
| *Flucelvax (influenza virus vaccine)* | *Novartis Vaccines and Diagnostics, Inc.* | Y | First | 11.9 | AP | 11.9 | Y+ |
| Epaned (enalapril maleate) | Silvergate Pharmaceuticals, Inc. | N | First | 9.9 | CR | 9.9 | Y |
| | | | Sponsor | 0.2 | -- | 10.1 | -- |
| | | | Second | 2.0 | AP | 12.1 | Y▲ |
| Desvenlafaxine Extended Release Tablets, 50 Mg And 100 Mg | Alembic Pharmaceuticals Ltd | N | First | 9.8 | TA | 9.8 | Y |
| | | | Sponsor | 0.5 | -- | 10.3 | -- |
| | | | Second | 2.0 | AP | 12.3 | Y▲ |
| Xeljanz (tofacitinib) | Pfizer, Inc. | Y | First | 12.6 | AP | 12.6 | Y+ |
| Gattex (teduglutide) | NPS Pharmaceuticals, Inc. | Y | First | 12.7 | AP | 12.7 | Y+ |
| *Octaplas (pooled plasma, solvent/detergent treated)* | *Octapharma Pharmazeutika Produktionsges.mbH* | Y | First | 12.8 | AP | 12.8 | Y+ |
| *Kcentra (prothrombin complex concentrate)* | *CSL Behring GmbH* | Y | First | 13.0 | AP | 13.0 | Y+ |
| Procysbi (cysteamine bitartrate) | Raptor Pharmaceuticals Corp | N | First | 13.0 | AP | 13.0 | Y+ |

* These submissions met the review goal, but due to rounding, they appear overdue.

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2012*** | | | | | | | |
| Docetaxel Injection | Actavis, Inc. | N | First | 13.0 | AP | 13.0 | Y+ |
| Suclear (sodium sulfate, potassium sulfate, and magnesium sulfate) | Braintree Laboratories, Inc. | N | First | 13.0 | AP | 13.0 | Y+ |
| Uceris (budesonide) | Santarus, Inc. | N | First | 13.0 | AP | 13.0 | Y+ |
| Sitavig (acyclovir) | Bioalliance Pharma SA | N | First | 13.0 | AP | 13.0 | Y+ |
| Tecfidera (dimethyl fumarate) | Biogen Idec, Inc. | Y | First | 13.0 | AP | 13.0 | Y+ |
| Versacloz (clozapine) | Jazz Pharmaceuticals International | N | First | 13.1 | AP | 13.1 | Y+* |
| Skyla (levonorgestrel-releasing intrauterine system) | Bayer Healthcare Pharmaceuticals, Inc. | N | First | 13.1 | AP | 13.1 | Y+* |
| Ravicti (glycerol phenylbutyrate) | Hyperion Therapeutics, Inc. | N | First | 13.4 | AP | 13.4 | N+ |
| Kazano (alogliptin and metformin hydrochloride) | Takeda Pharmaceuticals USA, Inc. | N | First | 14.2 | AP | 14.2 | N+ |
| (cyclophosphamide capsule) | Roxane Laboratories, Inc. | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 2.5 | -- | 12.5 | -- |
| | | | Second | 2.0 | AP | 14.5 | Y▲ |
| Tobi Podhaler (tobramycin inhalation powder | Novartis Pharmaceuticals Corp | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 1.3 | -- | 11.3 | -- |
| | | | Second | 3.8 | AP | 15.1 | Y△ |
| Zoledronic Acid Injection | Hospira, Inc. | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 1.3 | -- | 11.3 | -- |
| | | | Second | 5.8 | TA | 17.1 | Y△ |
| Zoledronic Acid Injection | ACS Dobfar Info SA | N | First | 10.0 | TA | 10.0 | Y |
| | | | Sponsor | 2.0 | -- | 12.0 | -- |
| | | | Second | 1.7 | CR | 13.7 | Y▲ |
| | | | Sponsor | 3.1 | -- | 16.8 | -- |
| | | | Third | 2.0 | AP | 18.8 | Y▲ |
| Injectafer (ferric carboxymaltose injection) | Luitpold Pharmaceuticals, Inc. | N | First | 9.7 | CR | 9.7 | Y |
| | | | Sponsor | 6.3 | -- | 16.0 | -- |
| | | | Second | 5.8 | AP | 21.8 | Y△ |

* These submissions met the review goal, but due to rounding, they appear overdue.

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2011*** | | | | | | | |
| Lamivudine/Tenofovir Disoproxil Fumarate Tablets, 300mg/300mg | Macleods Pharmaceuticals Ltd | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 1.1 | -- | 11.1 | -- |
| | | | Second | 6.1 | TA | 17.2 | Y△◊* |
| Abilify Maintena (aripiprazole) | Otsuka Pharmaceutical Co Ltd | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 1.2 | -- | 11.2 | -- |
| | | | Second | 6.0 | AP | 17.2 | Y△ |
| (testosterone 1% gel) | Perrigo Israel Pharmaceuticals Ltd | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 3.0 | -- | 13.0 | -- |
| | | | Second | 6.0 | AP | 19.0 | Y△ |
| Lymphoseek (tilmanocept) | Navidea Biopharmaceuticals, Inc. | Y | First | 13.1 | CR | 13.1 | Y+* |
| | | | Sponsor | 1.7 | -- | 14.8 | -- |
| | | | Second | 4.4 | AP | 19.2 | Y△ |
| Bethkis (tobramycin) | Cornerstone Therapeutics, Inc. | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 7.6 | -- | 17.6 | -- |
| | | | Second | 6.0 | AP | 23.6 | Y△ |
| Liptruzet (ezetimibe/atorvastatin) | Merck Sharp And Dohme Corp | N | First | 10.1 | CR | 10.1 | Y* |
| | | | Sponsor | 8.2 | -- | 18.3 | -- |
| | | | Second | 5.9 | AP | 24.2 | Y△ |
| *Evarrest (fibrin sealant patch)* | *Ethicon, Inc.* | Y | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 6.4 | -- | 16.4 | -- |
| | | | Second | 5.9 | CR | 22.3 | Y△ |
| | | | Sponsor | 0.4 | -- | 22.7 | -- |
| | | | Third | 1.9 | AP | 24.6 | Y▲ |
| Valchlor (mechlorethamine) | Ceptaris Therapeutics, Inc. | N | First | 9.3 | CR | 9.3 | Y |
| | | | Sponsor | 9.8 | -- | 19.1 | -- |
| | | | Second | 5.8 | AP | 24.9 | Y△ |

* These submissions met the review goal, but due to rounding, they appear overdue.

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2011*** | | | | | | | |
| *Bivigam (immune globulin intravenous)* | *Biotest Pharmaceuticals Corporation* | Y | First | 9.9 | CR | 9.9 | Y |
| | | | Sponsor | 1.8 | -- | 11.8 | -- |
| | | | Second | 6.0 | CR | 17.8 | Y△ |
| | | | Sponsor | 1.4 | -- | 19.1 | -- |
| | | | Third | 2.0 | CR | 21.1 | Y▲ |
| | | | Sponsor | 2.7 | -- | 23.8 | -- |
| | | | Fourth | 1.8 | AP | 25.5 | Y▲ |
| Zecuity (sumatriptan) | Nupathe, Inc. | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 10.6 | -- | 20.6 | -- |
| | | | Second | 6.1 | AP | 26.7 | Y△* |
| Lamivudine And Tenofovir Df Tablets, 300 Mg/300 Mg | Ranbaxy Laboratories Ltd | N | First | 27.6 | TA | 27.6 | N◊[9] |
| Karbinal ER (carbinoxamine maleate) | Tris Pharma, Inc. | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 12.0 | -- | 22.0 | -- |
| | | | Second | 5.7 | AP | 27.7 | Y△ |
| Suprax (cefixime) | Lupin Ltd | N | First | 10.0 | CR | 10.0 | Y |
| | | | Sponsor | 11.8 | -- | 21.8 | -- |
| | | | Second | 6.1 | AP | 27.9 | Y△* |
| (esomeprazole strontium) | Hanmi USA, Inc. | N | First | 13.0 | CR | 13.0 | Y+ |
| | | | Sponsor | 11.5 | -- | 24.5 | -- |
| | | | Second | 5.9 | TA | 30.4 | Y△ |
| | | | Sponsor | 1.2 | -- | 31.7 | -- |
| | | | Third | 2.0 | AP | 33.7 | Y▲ |

* These submissions met the review goal, but due to rounding, they appear overdue.

[9] During the review of this application, the applicant was under the Applications Integrity Policy (AIP) for a period of 16.8 months. Although FDA deferred substantive scientific review of the application during that period, the time is still included in calculations of cycle time. Excluding the time that the application was under AIP, FDA's review time was 10.8 months.

| Proprietary Name (established name) | Applicant | NME (Y/N) | Review Cycle | Cycle Time (mos.) | Cycle Result | Total Time (mos.) | Goal Met |
|---|---|---|---|---|---|---|---|
| ***Submitted in FY 2010*** | | | | | | | |
| Staccato (loxapine) | Teva Pharmaceuticals USA, Inc. | N | First | 9.9 | CR | 9.9 | Y |
| | | | Sponsor | 9.9 | -- | 19.8 | -- |
| | | | Second | 9.0 | CR | 28.8 | Y∆+ |
| | | | Sponsor | 1.6 | -- | 30.4 | -- |
| | | | Third | 6.0 | AP | 36.4 | Y∆ |
| ***Submitted in FY 2009*** | | | | | | | |
| Topotecan Hydrochloride Injection | Teva Pharmaceuticals USA | N | First | 9.9 | CR | 9.9 | Y |
| | | | Sponsor | 32.3 | -- | 42.2 | -- |
| | | | Second | 5.9 | AP | 48.1 | Y∆ |
| ***Submitted in FY 2008*** | | | | | | | |
| Oseni (alogliptin and pioglitazone) | Takeda Pharmaceuticals USA, Inc. | N | First | 11.4 | CR | 11.4 | N |
| | | | Sponsor | 22.7 | -- | 34.1 | -- |
| | | | Second | 9.1 | CR | 43.2 | Y∆+* |
| | | | Sponsor | 3.1 | -- | 46.3 | -- |
| | | | Third | 6.0 | AP | 52.3 | Y∆ |
| Nesina (alogliptin) | Takeda Pharmaceuticals USA, Inc. | Y | First | 18.0 | CR | 18.0 | N |
| | | | Sponsor | 25.0 | -- | 43.0 | -- |
| | | | Second | 9.1 | CR | 52.1 | Y∆+* |
| | | | Sponsor | 3.0 | -- | 55.1 | -- |
| | | | Third | 6.0 | AP | 61.1 | Y∆ |
| Zegerid OTC (omeprazole 20mg & sodium bicarbonate 1680mg) | MSD Consumer Care, Inc. | N | First | 9.9 | CR | 9.9 | Y |
| | | | Sponsor | 11.9 | -- | 21.8 | -- |
| | | | Second | 5.9 | CR | 27.7 | Y∆ |
| | | | Sponsor | 11.6 | -- | 39.3 | -- |
| | | | Third | 6.0 | CR | 45.3 | Y∆ |
| | | | Sponsor | 11.7 | -- | 57.0 | -- |
| | | | Fourth | 6.0 | AP | 63.0 | Y∆ |

* These submissions met the review goal, but due to rounding, they appear overdue.

# Appendix D: Filed Application Numbers by Review Division

The tables below and on the pages that follow show the number of applications filed in FY 2013 for various application types and review designations broken out by review division. This new reporting for PDUFA V is required under Section 104 of FDASIA.

## Original Applications Filed in FY 2013 by Review Division (CDER)

| Review Division/Office | Priority NDAs | Standard NDAs | Priority BLAs | Standard BLAs | Undesignated Original Applications |
|---|---|---|---|---|---|
| **CDER Review Divisions** | | | | | |
| Division of Anesthesia, Analgesia, and Addiction Products | 3 | 6 | 0 | 0 | 0 |
| Division of Anti-Infective Products | 3 | 6 | 0 | 0 | 0 |
| Division of Antiviral Products | 6 | 6 | 0 | 0 | 0 |
| Division of Bone, Reproductive, and Urologic Products | 0 | 5 | 0 | 0 | 0 |
| Division of Cardiovascular and Renal Products | 1 | 11 | 0 | 1 | 0 |
| Division of Dermatology and Dental Products | 0 | 7 | 0 | 0 | 0 |
| Division of Gastroenterology and Inborn Errors Products | 2 | 5 | 2 | 1 | 0 |
| Division of Hematology Products | 1 | 6 | 2 | 2 | 0 |
| Division of Medical Imaging Products | 0 | 4 | 0 | 0 | 0 |
| Division of Metabolism and Endocrinology Products | 0 | 8 | 1 | 2 | 0 |
| Division of Neurology Products | 1 | 4 | 0 | 1 | 0 |
| Division of Nonprescription Clinical Evaluation | 0 | 7 | 0 | 0 | 0 |
| Division of Oncology Products 1 (DOP1) | 1 | 0 | 0 | 0 | 0 |
| Division of Oncology Products 2 (DOP2) | 1 | 0 | 1 | 0 | 0 |
| Division of Psychiatry Products | 0 | 8 | 0 | 0 | 0 |
| Division of Pulmonary, Allergy, and Rheumatology Products | 0 | 8 | 0 | 1 | 0 |
| Division of Transplant and Ophthalmology Products | 1 | 3 | 0 | 0 | 0 |
| *CDER Totals* | *20* | *94* | *6* | *8* | *0* |

## Original Applications Filed in FY 2013 by Review Office (CBER)

| Review Division/Office | Priority NDAs | Standard NDAs | Priority BLAs | Standard BLAs | Undesignated Original Applications |
|---|---|---|---|---|---|
| **CBER Review Offices** | | | | | |
| Office of Blood Research and Review | 0 | 0 | 2 | 6 | 0 |
| Office of Cellular Tissue and Gene Therapies | 0 | 0 | 0 | 0 | 0 |
| Office of Vaccines Research and Review | 0 | 0 | 0 | 0 | 0 |
| *CBER Totals* | *0* | *0* | *2* | *6* | *0* |
| **FDA Totals** | **20** | **94** | **8** | **14** | **0** |

## Efficacy Supplements Filed in FY 2013 by Review Division/Office

| Review Division/Office | Priority Efficacy Supplements | Standard Efficacy Supplements | Undesignated Efficacy Supplements |
|---|---|---|---|
| **CDER Review Divisions** | | | |
| Division of Anesthesia, Analgesia, and Addiction Products | 3 | 2 | 0 |
| Division of Anti-Infective Products | 0 | 1 | 0 |
| Division of Antiviral Products | 7 | 5 | 0 |
| Division of Bone, Reproductive, and Urologic Products | 0 | 9 | 0 |
| Division of Cardiovascular and Renal Products | 1 | 6 | 0 |
| Division of Dermatology and Dental Products | 0 | 1 | 0 |
| Division of Gastroenterology and Inborn Errors Products | 1 | 9 | 1 |
| Division of Hematology Products | 1 | 4 | 2 |
| Division of Medical Imaging Products | 0 | 1 | 0 |
| Division of Metabolism and Endocrinology Products | 0 | 6 | 0 |
| Division of Neurology Products | 3 | 17 | 0 |
| Division of Nonprescription Clinical Evaluation | 0 | 3 | 0 |
| Division of Oncology Products 1 (DOP1) | 2 | 3 | 0 |
| Division of Oncology Products 2 (DOP2) | 7 | 4 | 0 |
| Division of Psychiatry Products | 0 | 6 | 0 |
| Division of Pulmonary, Allergy, and Rheumatology Products | 1 | 16 | 0 |
| Division of Transplant and Ophthalmology Products | 0 | 2 | 0 |
| *CDER Totals* | *26* | *95* | *3* |
| **CBER Review Offices** | | | |
| Office of Blood Research and Review | 1 | 7 | 0 |
| Office of Cellular Tissue and Gene Therapies | 0 | 0 | 0 |
| Office of Vaccines Research and Review | 0 | 10 | 0 |
| *CBER Totals* | *1* | *17* | *0* |
| **FDA Totals** | **27** | **112** | **3** |

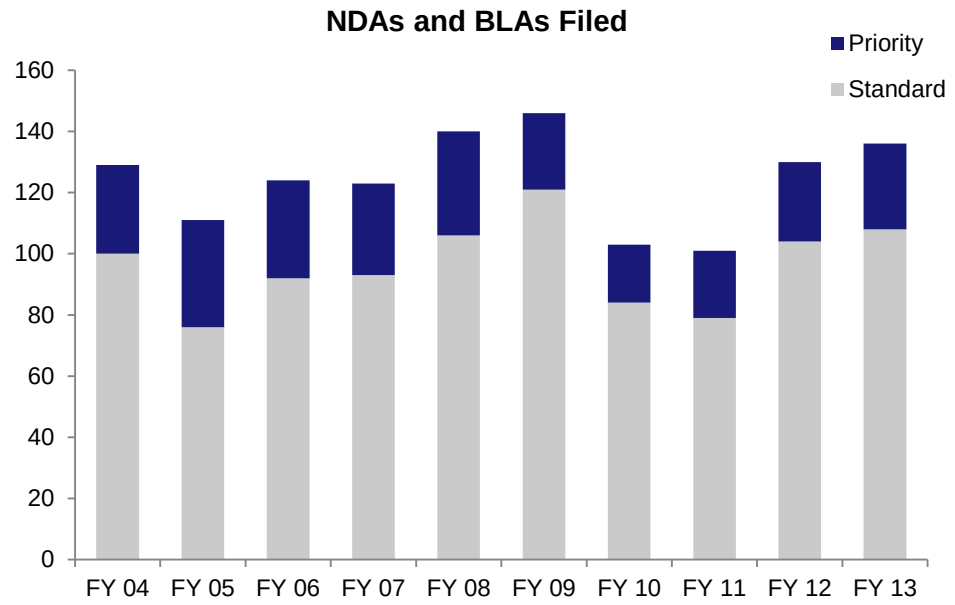
## Submissions with Special Designations Filed in FY 2013 by Review Division

| Review Division/Office | Accelerated Approval | Fast Track Products | Orphan Designations | Breakthrough Designations* |
|---|---|---|---|---|
| **CDER Review Divisions** | | | | |
| Division of Anesthesia, Analgesia, and Addiction Products | 0 | 0 | 0 | 0 |
| Division of Anti-Infective Products | 0 | 2 | 1 | 0 |
| Division of Antiviral Products | 0 | 8 | 0 | 7 |
| Division of Bone, Reproductive and Urologic Products | 0 | 0 | 0 | 0 |
| Division of Cardiovascular and Renal Products | 0 | 2 | 3 | 1 |
| Division of Dermatology and Dental Products | 0 | 0 | 0 | 1 |
| Division of Gastroenterology and Inborn Errors Products | 0 | 3 | 3 | 2 |
| Division of Hematology Products | 1 | 1 | 4 | 7 |
| Division of Medical Imaging Products | 0 | 0 | 0 | 0 |
| Division of Metabolism and Endocrinology Products | 0 | 1 | 1 | 0 |
| Division of Neurology Products | 0 | 1 | 3 | 3 |
| Division of Nonprescription Clinical Evaluation | 0 | 0 | 0 | 0 |
| Division of Oncology Products 1 (DOP1) | 0 | 1 | 0 | 2 |
| Division of Oncology Products 2 (DOP2) | 0 | 1 | 2 | 3 |
| Division of Psychiatry Products | 0 | 0 | 0 | 0 |
| Division of Pulmonary, Allergy, and Rheumatology Products | 0 | 0 | 0 | 2 |
| Division of Transplant and Ophthalmology Products | 0 | 0 | 2 | 0 |
| *CDER Totals* | *1* | *20* | *19* | *28* |
| **CBER Review Offices** | | | | |
| Office of Blood Research and Review | 0 | 0 | 6 | 0 |
| Office of Cellular Tissue and Gene Therapies | 0 | 0 | 0 | 0 |
| Office of Vaccines Research and Review | 0 | 0 | 0 | 0 |
| *CBER Totals* | *0* | *0* | *6* | *0* |
| **FDA Totals** | **1** | **20** | **25** | **28** |

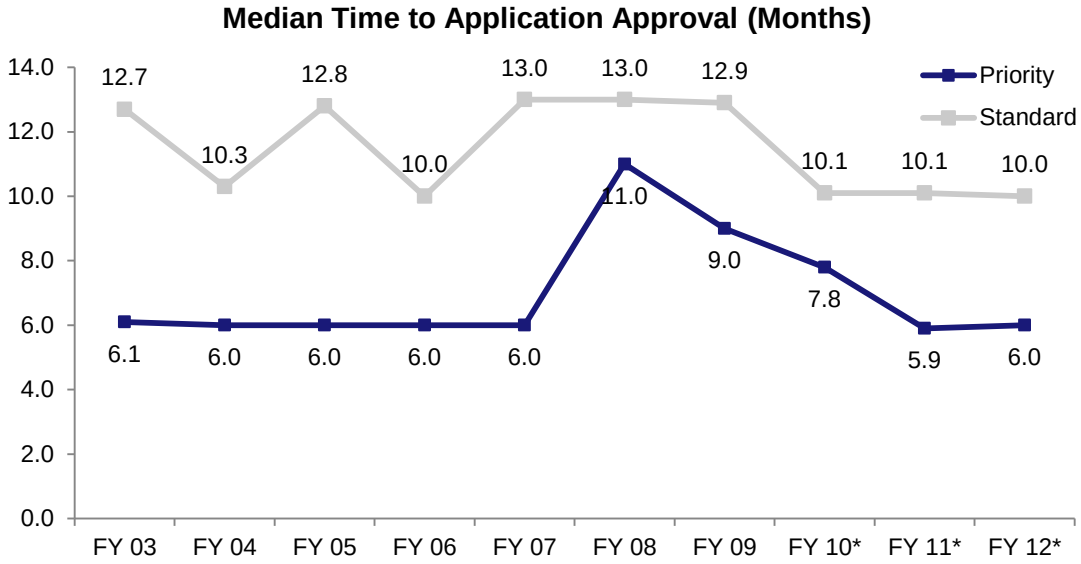
* This column does not represent filed figures; rather it shows the number of breakthrough designations granted on INDs, NDAs, and BLAs during FY 2013. Breakthrough designation is granted based on indication, and therefore one submission may have more than one breakthrough designation granted.

# Appendix E: PDUFA Trend Graphs

The number of NDAs and BLAs filed from FY 2004 to FY 2013 is presented in the graph below. The number of applications in FY 2013 increased to a 4-year high.

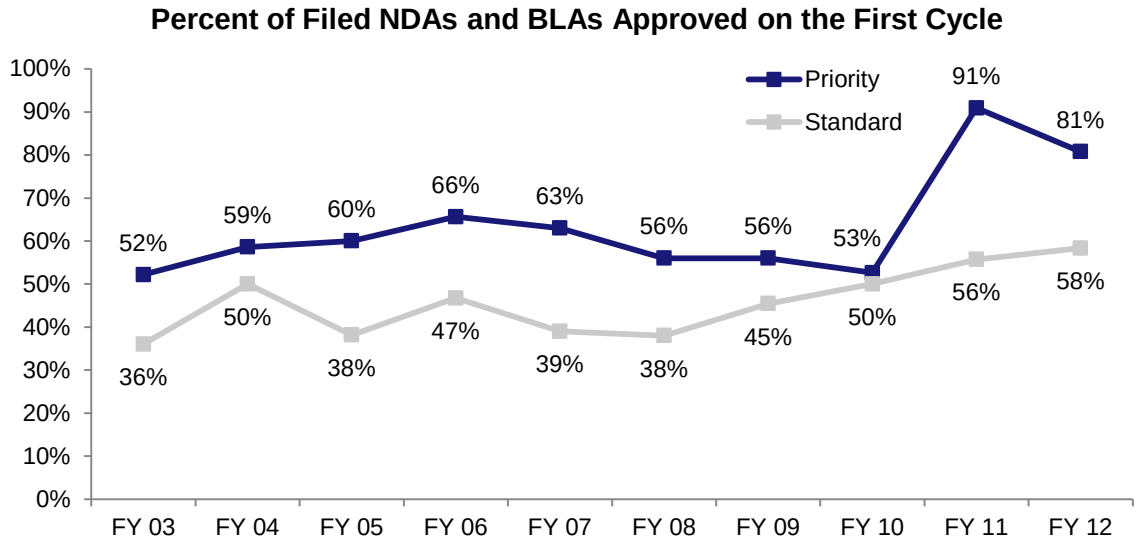



Median total time to approval for priority and standard applications for FY 2003 through FY 2012 are presented in the graph below. Median approval times for both priority and standard applications in FY 2012 reached median approval times equal to the review-time goals for their respective submission types. This is consistent with the greater than 50 percent rate of approvals in the first review cycle for both application types (see graph on the following page). FY 2013 data are too preliminary to estimate the median approval time.




* The median approval times for the three most recent years are estimated.

The percentages of first-cycle approvals for priority and standard NDAs and BLAs filed from FY 2003 to FY 2012 are presented in the graph below. First-cycle approvals for priority NDAs and BLAs reached a 10-year high in FY 2011, with 91 percent of applications approved on the first cycle, and remained high in FY 2012, with 81 percent of applications approved on the first cycle. Standard applications have seen a steady increase in first-cycle approvals since FY 2008, reaching a 10-year high in FY 2012 with 58 percent of applications approved on the first cycle. FY 2013 data is too preliminary to estimate the percent of first-cycle approvals.



# Appendix F: Definitions of Key Terms

A. The term "review and act on" means the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval.

B. Goal Date Extensions for Major Amendments

1. A major amendment to an original application, efficacy supplement, or Class 2 resubmission of any of these applications, submitted at any time during the review cycle, may extend the goal date by 3 months. [Note: If the review cycle occurred prior to FY 2013, the major amendment must have been received within 3 months of the action due date to extend the action goal date by 3 months.]
2. A major amendment may include, for example, a major new clinical safety/efficacy study report; major re-analysis of previously submitted study(ies); submission of a REMS with elements to assure safe use (ETASU) not included in the original application; or significant amendment to a previously submitted REMS with ETASU. Generally, changes to REMS that do not include ETASU and minor changes to REMS with ETASU will not be considered major amendments.
3. A major amendment to a manufacturing supplement submitted at any time during the review cycle may extend the goal date by 2 months. [Note: If the review cycle occurred prior to FY 2013, the major amendment must have been received within 2 months of the action due date to extend the action goal date by 2 months.]
4. Only one extension can be given per review cycle.
5. Consistent with the underlying principles articulated in the Good Review Management Principles (GRMP) guidance, FDA's decision to extend the review clock should, except in rare circumstances, be limited to occasions where review of the new information could address outstanding deficiencies in the application and lead to approval in the current review cycle.

C. A resubmitted original application is a complete response to an action letter addressing all identified deficiencies.

D. Class 1 resubmitted applications are applications resubmitted after a complete response letter (or a not approvable or approvable letter) that include the following items only (or combinations of these items):

1. Final printed labeling
2. Draft labeling
3. Safety updates submitted in the same format, including tabulations, as the original safety submission with new data and changes highlighted (except when large amounts of new information, including important new adverse experiences not previously reported with the product, are presented in the resubmission)
4. Stability updates to support provisional or final dating periods
5. Commitments to perform Phase 4 postmarketing studies, including proposals for such studies
6. Assay validation data
7. Final release testing on the last 1-2 lots used to support approval
8. A minor reanalysis of data previously submitted to the application (determined by the agency as fitting the Class 1 category)
9. Other minor clarifying information (determined by the agency as fitting the Class 1 category)

10. Other specific items may be added later as the agency gains experience with the scheme and will be communicated via guidance documents to industry

E. Class 2 resubmissions are resubmissions that include any other items, including any item that would require presentation to an advisory committee.

F. Meeting requests commit FDA to notify the requestor of a formal meeting in writing within 14 days of request for Type A meetings or within 21 days of request for Type B and Type C meetings.

G. Scheduled meetings should be made within 30 days of receipt of request for Type A meetings, 60 days for Type B meetings, and 75 days for Type C meetings. If the requested date for any of these types of meetings is greater than 30, 60, or 75 days, as appropriate, from the date the request is received by FDA, the meeting date should be within 14 days of the requested date.

H. Meeting minutes are to be prepared by FDA clearly outlining agreements, disagreements, issues for further discussion, and action items. They will be available to the sponsor within 30 days of the meeting.

I. A Type A Meeting is a meeting that is necessary for an otherwise stalled drug development program to proceed (a "critical path" meeting) or to address an important safety issue.

J. A Type B Meeting is a: 1) pre-IND, 2) end of Phase 1 (for Subpart E or Subpart H or similar products) or end of Phase 2/pre-Phase 3, or 3) a pre-NDA/BLA meeting. Each requestor should usually only request one of these Type B Meetings for each potential application (NDA/BLA) (or combination of closely related products, i.e., same active ingredient, but different dosage forms being developed concurrently).

K. A Type C Meeting is any other type of meeting.

L. The performance goals and procedures also apply to original applications and supplements for human drugs initially marketed on an over-the-counter (OTC) basis through an NDA or switched from prescription to OTC status through an NDA or supplement.

M. IT-specific definitions:

1. "Program" refers to the organizational resources, procedures, and activities assigned to conduct "the process for the review of human drug applications," as defined in the Prescription Drug User Fee Act.
2. "Standards-based" means compliant with published specifications that address terminology or information exchange between FDA and regulated parties or external stakeholders, as adopted by FDA or other agencies of the federal government, and often based on the publications of national or international Standards Development Organizations.
3. "FDA Standards" means technical specifications that have been adopted and published by the FDA through the appropriate governance process. FDA standards may apply to terminology, information exchange, engineering or technology specifications, or other technical matters related to information systems. FDA standards often are based on the publications of other federal agencies or the publications of national or international Standards Development Organizations.
4. "Product life cycle" means the sequential stages of human drug development, regulatory review and approval, post-market surveillance and risk management, and where applicable, withdrawal of an approved drug from the market. In the context of the process for the review of human drug applications, the product life cycle begins with the earliest regulatory submissions in the IND phase, continues through the NDA or BLA review phase, and includes post-market surveillance and risk management activities as covered under the process for the review of human drug applications.

N. Special Protocol Assessments: Upon specific request by a sponsor, FDA will evaluate certain protocols and issues to assess whether the design is adequate to meet scientific and regulatory requirements identified by the sponsor.

O. First Cycle Filing Review Notifications: Under PDUFA V, FDA committed to report 90 percent of substantive review issues (or lack thereof) identified during the initial filing review to the applicant by letter, telephone conference, facsimile, secure e-mail, or other expedient means within 74 days of receipt of the original submission.

P. Planned Review Timeline Notifications: FDA is to inform the applicant of the planned timeline for feedback related to labeling and PMRs/PMCs. Beginning in FY 2013, applications being reviewed under the Program are to include additional information about the planned date for the internal mid-cycle meeting and preliminary plans on whether to hold an advisory committee meeting to discuss the application.

Q. The Application Integrity Policy focuses on the integrity of data and information in applications submitted to FDA for review and approval. It describes FDA's approach regarding the review of application that may be affected by wrongful acts that raise significant questions regarding data reliability. More information on the policy is available at http://www.fda.gov/downloads/ICECI/EnforcementActions/ApplicationIntegrityPolicy/UCM072631.pdf.


**Department of Health and Human Services**
**Food and Drug Administration**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